Biotie Therapies

Initial Report

Favorable risk-return profile

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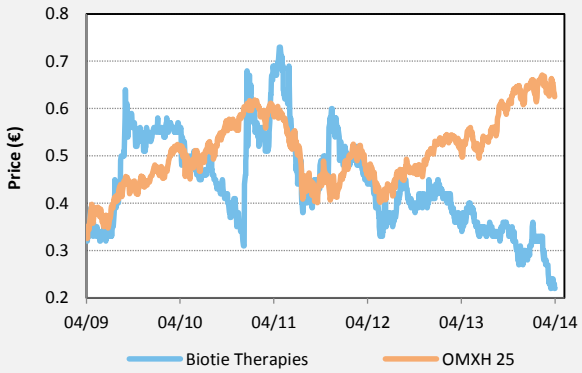
Initial report

- Biotie is a specialized drug development company focused on products for neurodegenerative and psychiatric disorders. The company has an interesting development pipeline, holding treatments with very high market potential. Biotie has a solid financial position and at present a relatively low cash burn rate, but due to the nature of the drug development process the risk profile of the investment case is high.
- Biotie's spearhead product is Selincro for alcohol dependence. Biotie's partner Lundbeck launched Selincro in several markets in Europe in 2013. While we believe that Selincro is the most valuable product of Biotie at the moment, tozadenant (for Parkinson's disease) and SYN120 (for Alzheimer's disease) hold an even larger potential than it. These products are in the development pipeline and it will probably take in excess of 5 years before they could reach the markets; the probability of success isn't high. Still, the market opportunity is so large that they have significant value even with the high risks.
- We believe Biotie's current fair value to be around 145 M€. The value is driven mostly by Selincro (rNPV of 87 M€), tozadenant (rNPV of 47 M€) and SYN120 (rNPV of 25 M€). Our short term focus is on tozadenant, as Biotie needs to find a partner before progressing to Phase 3 development. Our recommendation is buy with a target price of 0.32 euros. We note that Biotie is a very high risk investment, but the upside potential in a positive scenario is very rewarding.



Share price, EUR (last close)	**0.22**
Target price, EUR	0.32
No. of shares, '000's	456 032
Market cap, MEUR	100.3
Ticker	BTH1V
Bloomberg code	BTH1V.FH
Next interim report	May 9, 2014
Web site	www.biotie.com

Investment profile

Potential	Very large if R&D successful
Risk profile	Very high; medical R&D risks
Investment profile	High risk, high reward Do not expect dividends

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Key figures

Market cap, MEUR	100	BV per share 2013E, EUR	0.18	EPS 2013, EUR	0.01
Liquid assets 2013, MEUR	44	Price/book 2013	1.6	Revenue 2013, MEUR	27.7
Equity ratio (%) 2013	69.2 %	Dividend yield 2013, %	0.0	Operative cash flow 2013, MEUR	10.9
Equity 2013, MEUR	80.8	Tax rate 2013, %	0.0	Total assets 2013, MEUR	120.4

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Investment case summary

Biotie is a specialized drug development company focused primarily on products for neurodegenerative and psychiatric disorders. It is a small company and it is natural that it has focused in specific areas. The company's strategy has been built on the "search, profile and partner" approach. After the recent change in strategy, Biotie is also looking for opportunities to take specific treatments to the market independently. Biotie's main income streams are milestone payments and royalties from the sales of products.

Biotie's financial position is currently solid. At the end of the year the company has roughly 44 MEUR in cash, which gives it a very comfortable buffer for the future. Biotie has reasonably good prospects in milestone payments and royalties, but it will burn cash especially in the development of SYN120 (progressing to Phase 2). Our short-term focus is on the partnering situation of tozadenant; Biotie needs to find a new partner to replace UCB Pharma, as they recently decided to return the rights to the company. Tozadenant should be progressing to Phase 3 soon and Biotie cannot independently finance the expenses of >100 MEUR. Before the company can find a new partner, hopefully a credible large pharma company, the risk level associated with tozadenant will be elevated. This also puts pressure on the share price on short term.

The value of Biotie derives from its product portfolio; more accurately the intellectual property rights (IPR) to these drugs. Biotechnology is a business of IPR above anything else. It's also a high risk business, as development of new drugs is very expensive and includes very significant risks (only 1/10000 of researched, potential drugs is very successful). On the other hand, the potential value of a successful drug is huge. The gross margins of medicines are extremely high during the patent protection time; this is the period when companies make the money back. Considering the nature of the industry, we would use the analogy of start-up investing. The management faces a lot of similar decisions as a portfolio manager in the start-up sector.

Biotie, or any other small biotech company, is not for a risk-averse investor. There's a potentially huge upside, but the risks are also very high. Because the development periods of new drugs are on average 10-15 years, investing in Biotie also requires a lot of patience. It's worth noting that quarterly earnings are almost meaningless in this business sector. Favorable research results bring value to the products even though revenues still won't occur for a long time. Thereby we advise investors to focus on the long term development of the products and our investment case.

Biotie is a small and specialized drug development company focused primarily on products for neurodegenerative and psychiatric disorders.

The company's strategy has been built on the "search, profile and partner" approach. After the recent change in strategy, Biotie is also looking for opportunities to take specific treatments to the market independently.

Biotie's main income streams are milestone payments and royalties from the sales of products and its financial position is currently solid.

The value of Biotie derives from its product portfolio. Biotie is not for a risk-averse investor. There's a potentially huge upside, but the risks are also very high.

Product pipeline in a nutshell

Biotie's product portfolio currently consists of five medications in different development phases. Out of these Selincro (for alcohol dependence) has been launched in Europe and currently is also the company's most valuable product in our opinion. We see significant potential in tozadenant, which is a currently phase 3-ready medicine for Parkinson's disease. Also SYN120 for Alzheimer's disease would be very valuable if successful. At the present, Biotie is preparing SYN120 for phase 2 studies. We believe that these three afore mentioned products hold over 90 % of the value of Biotie, and we will be focusing on them in this report.

Biotie's lead product Selincro (nalmefene) is an orally administered opioid receptor ligand for the treatment of alcohol dependence. Selincro is approved in Europe for the reduction of alcohol consumption of adult patients suffering from alcohol dependence. While the prevalence of alcoholism is relatively high and there are probably more than 15 million people suffering from it only in Europe, the nature of the disease makes it a commercially challenging market. This clearly limits the market potential and creates commercial risk. Selincro is also a paradigm shifting drug, because it is currently the only drug for the reduction of alcohol consumption instead of complete abstinence. The efficacy of Selincro has been good and we believe it to be successful, providing it can get the necessary reimbursement decisions in the key markets, as well as high acceptance among doctors. We believe that Selincro's value is around 88 MEUR (calculated with rNPV).

We believe that tozadenant (for Parkinson's disease) and SYN120 (for Alzheimer's disease) which are still in the development pipeline clearly hold larger potential than Selincro. Both Parkinson's and

Biotie's product portfolio currently consists of five medications in different development phases.

Selincro (for alcohol dependence) is the only one that has been launched in Europe and currently is also the company's most valuable product in our opinion. We believe that Selincro's value is around 88 MEUR.

We see significant potential in tozadenant, which is a currently phase 3-ready medicine for Parkinson's disease. The Phase 2 studies of tozadenant provided strong results in efficacy and

Alzheimer's disease are huge in terms of market size and any medicine that can bring significant benefits to the patients has very high value.

Tozadenant (SYN115) is a novel product for Parkinson´s disease; it has unique mechanisms of action and could be a first-in-class inhibitor of the adenosine 2a (A2a) receptor. There are naturally some competitors in the huge PD market, but the Phase 2 data of tozadenant has been promising and the drug has very substantial potential. The Phase 2 studies of tozadenant provided strong results in efficacy and we believe that the drug has a good potential to succeed. However, the partnering and financing situation creates additional uncertainty for tozadenant. Recently the development of tozadenant suffered a significant setback, because UCB decided to return the global rights to tozadenant to Biotie. The partnering situation should be resolved soon after the FDA end-of-phase 2 meeting that is scheduled for H1'14. If everything were to progress well, tozadenant could be launched to the markets around the year 2020. The value of tozadenant is still only "potential" and the probability of success is relatively low (when including clinical, commercial, financial and partnering risks). Still the large potential, if successful, is so high that we believe the current rNPV to be around 47 MEUR. In case of a breakthrough, it could be much higher. Significant value could be added only by reducing the risks and therefore increasing the probability of success, which we are now estimating to be only around 30 %.

SYN120 for Alzheimer's disease is another interesting possibility in the pipeline; it has a dual activity with significant differentiation from the many competitors. After lengthy partnering negations, Biotie decided to invest in SYN120 and is attempting to make it a phase 3-ready asset before partnering. Alzheimer's disease is the leading cause of dementia in the ageing population and represents a huge social and economic burden. The market opportunity regarding treatment of Alzheimer's is huge, but it is also a challenging market that has been called "graveyard of drug candidates" due to many large failures in the recent years. SYN120 is still far away in the development pipeline and it will probably take in excess of five years before it could reach the markets. The probability of success is low at this point, but if the development progresses positively, the value could increase considerably. Still, the market opportunity is so large that they have significant value (estimated to be around 25 MEUR currently), even with the high risks. We are currently giving SYN120 a probability of success of only 20 % due to clinical, financial and commercial risks – Biotie is investing its own money in the development process now, so the financial risk is also considerable.

We have presented some basic information on all the products of Biotie in the following table. The value of the products depend heavily on the assumptions on probability of success, royalties as well as estimated peak sales. These are naturally extremely difficult to estimate for drugs that are still in the development pipeline, so there's significant uncertainty regarding these estimates. We have tried to be cautious with our assumptions.

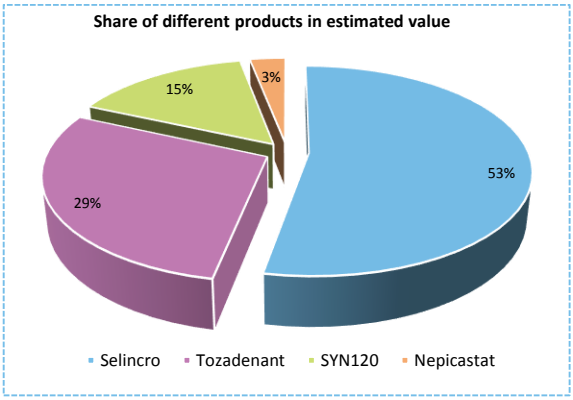
we believe that the drug has a good potential to succeed. However, the partnering and financing situation creates additional uncertainty for tozadenant. We believe the drug's value (rNPV) to be around 47 MEUR currently.

Also SYN120 for Alzheimer's disease would be very valuable if successful. At present, Biotie is preparing SYN120 for phase 2 studies, which means that its commercialization is still a "long shot". Still, the market opportunity is so large that it has have significant value (around 25 MEUR), even with the high risks.

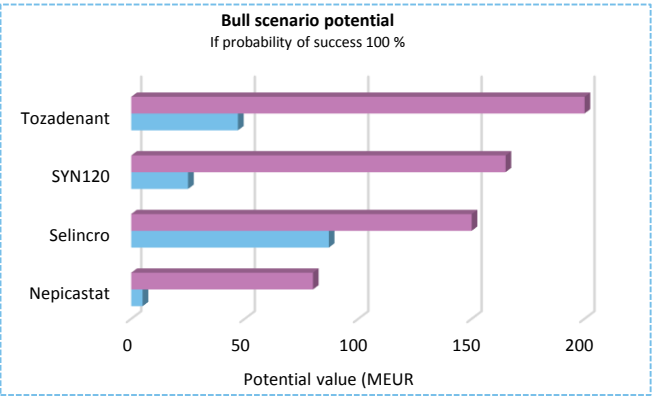
We believe that these three afore mentioned products hold over 90 % of the value of Biotie, and we will be focusing on them in this report.

Product	Status	Probability of success (%)	Estimated launch year	Estimated peak market share	Estimated royalty	Estimated peak sales	Patent expiry	Estimated value (rNPV)
Selincro (nalmefene) *Alcohol dependence*	Approved and launched in EU	75 % regarding commercial success	Launched in 2013	33 %	15 %	300 MEUR	2023	87 MEUR
Tozadenant (SYN115) *Parkinson's disease*	Phase 3-ready	Possible 30 % (partnering, clinical & commercial risks)	2020	Possible significant in terms of value	10 %	Easily higher than billion euros, if the profile is favorable	2031	47 MEUR
SYN120 - *Alzheimer's disease and other cognitive disorders.*	Phase 2-ready	Around 20 % (clinical, financial & commercial risks)	2020	Small - lots of competitors	12 %	Huge market potential	2030	25 MEUR
Nepicastat (SYN117) - *Cocaine dependence*	Phase 2 ongoing	5 %, very high risk due to the difficult target group	2020	So far no competitors	Possibility of independent launch	Small market, difficult to estimate	Unknown at this point	5 MEUR
BTT-1023 (VAP-1 antibody) *Fibrosis*	Phase 2-ready	10 %, still early in the pipeline	Will be evaluated after financing P2	Possible orphan medinicine	Too early to estimate	Small market, but possible high share	Unknown at this point	Value cannot be determined at this point
NRL-1 - option *Acute Repetitive Epileptic Seizures*	Phase 2-ready	0 %	Biotie didn't use the buy option	-	-	-	-	No value at this point

Table 1. *Biotie valuation model and key assumptions.* *Source: Inderes*



Graph 1. The estimated value distribution of Biotie. *Source: Inderes*



Graph 2. Illustration of the bull scenario potential. *Source: Inderes*

Summary of the key elements of our investment case

	Selincro	Tozadenant	SYN120
Value Drivers	• Launches to new markets (milestones for Biotie) • Reimbursement decisions • Sales of Selincro (royalties for Biotie) • Possible launch in Japan	• The end-of-Phase 2 meeting with FDA in H1'14 • Resolving the partnering and financing situation • Progressing to Phase 3 • Increasing the probability of successful launch	• Starting the Phase 2 trials • Positive data from P2 confirming the profile of the drug • Partnering when the drug has progressed to P3-ready status
Risks & Challenges	• Negative reimbursement decisions • Failure to reach high acceptance among GPs • Commercial letdown; unsatisfactory ramp-up of sales	• Either unsatisfactory partnership agreement or failure to reach a deal • Weak P3 data leading into "moderate" profile without significant additional benefits	• Failure to produce strong efficacy and safety data in P2 studies • Includes also significant financial risks for Biotie • Partnering risk if reaches the P3-ready status
Potential	Alcohol dependency is a relatively small market; estimated peak sales 300 MEUR. Still very important for Biotie.	Parkinson's disease is a huge market and any drug with substantial benefits to the patients should reach peak sales >1 BEUR	Alzheimer's disease is a huge market and any drug with substantial benefits to the patients should reach peak sales >1 BEUR

We believe that the potential of these products outweighs the high risks and therefore believe that Biotie is currently undervalued.

Recommendation	Buy
Target Price	0.32 EUR (next 12 months)

1. Biotie in a nutshell

Biotie is a specialized drug development company focused primarily on products for neurodegenerative and psychiatric disorders. While Biotie is naturally a biotechnology company, its business model has some analogies with high-risk investment companies (for example start-up funds), as well as expert or specialist organization models. They only have roughly 40 employees, but most of them could be considered as project managers who require high expertise in the medical development. Almost everything on the ground level has been outsourced.

During the past years, Biotie has successfully operated a strategy built around search, profile and partner. This has delivered Selincro (nalmefene) for alcohol dependency, which received European marketing authorization in February 2013 and is currently being rolled out across Europe by partner Lundbeck. The company's other key prospect is tozadenant, a novel A2a antagonist, which is in collaboration with UCB transitioning into Phase 3 development for Parkinson's disease.

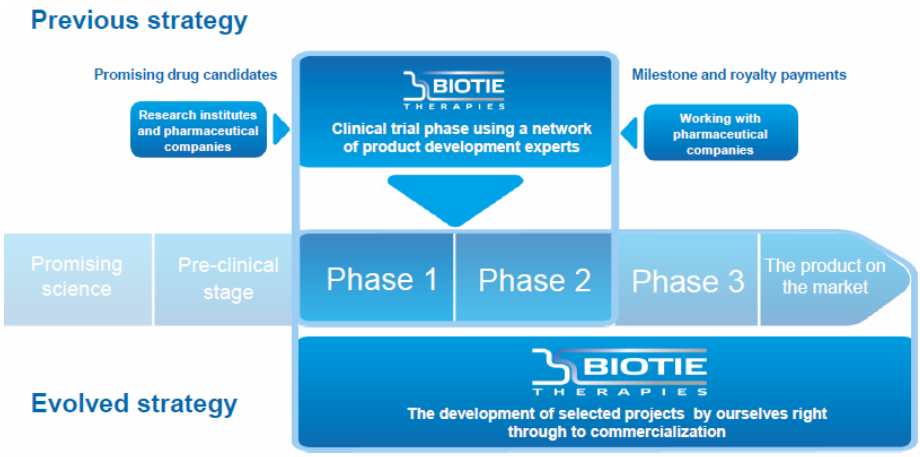
In addition to these, Biotie has three other medicines in the development pipeline, and the company plans to seek further opportunities to generate a strong portfolio of products. The company's MCAP is currently roughly 100 MEUR and its shares are listed on the Helsinki Stock Exchange.

Biotie is a specialized drug development company focused primarily on products for neurodegenerative and psychiatric disorders. It currently has five different drugs in its portfolio. Out of these Selincro has been launched.

Biotie is a biotech company that employs roughly 40 experts in the field of medical development.

1.1 Focus areas – Biotie is a CNS specialist

There are many different areas in the development process of medicine. Different stages require different expertise and resources, and there are only a few companies that still cover the whole value chain. Others have chosen to focus in different areas, where they feel that they can add the most value with a suitable risk profile. Biotie is a small company and it is natural that it has focused in certain areas. The company's strategy has been built around "search, profile and partner" approach. After the recent change in the strategy, Biotie is also looking for opportunities to take specific treatments to the market independently (see the following picture 1). Biotie is primarily focused on products for neurodegenerative and psychiatric disorders, which means that it has a relatively tight scope in its products.



Picture 1. *Biotie's evolving strategy.* *Source: Company materials*

With its search, profile and partner-strategy Biotie has focused mostly in the area of clinical studies (Phases 1 and 2 as well as partnering for 3). It is not involved in the discovery of new drugs or the pre-clinical research in general. This means that Biotie usually acquires the rights to its products after the pre-clinical studies or clinical phase 1. The company is mostly interested in products that have been found safe in the pre-clinical studies, having past at least Phase 1 and possibly also the Phase 2 clinical studies. We could say that Biotie is mostly focused on Phase 1 and Phase 2 studies as an independent company. In the revised strategy, the company stated that it also wants to take the products all the way to the market. If the product has a suitable profile, it's definitely a strategic option, but we believe that the company's partnering strategy is still valid in many cases.

Biotie is a small company and focused in certain areas of the drug development process.

The company's strategy has been built around the "search, profile and partner" approach. After the recent change in strategy, Biotie is also looking for opportunities to take specific treatments to the market by itself.

Biotie is not involved in the discovery of new drugs or pre-clinical research. We could say that Biotie is mostly focused on Phase 1 and Phase 2 studies as an independent company. In Phase 3, due to the high costs, a partnership is still a predominant option, though this depends on the profile of the drug. In general the company is focused in "value inflection points".

So far the company hasn't launched any products independently, but the company has now stated that it is prepared to do also this. However, we believe that the product should be specialized with a small enough target group in terms of marketing. Biotie doesn't possess the necessary resources to launch a product for a "general market" with a large number of call points. In our opinion, the product would be suitable if there's no need to reach a huge network of general practitioners (GP), but e.g. hospitals and specialized clinics instead. For example nepicastat, a medicine under development for cocaine dependence, could be targeted at a small group of specialists in this area. A general practitioner doesn't generally treat cocaine dependence; the patients are referred to a specialist.

So far the company hasn't launched any products to the markets without a partner, but it could do this if the drug has a suitable profile: specialized drug with centralized call points. For example nepicastat would facilitate this.

It is also worth noting that the company doesn't have to have the necessary resources to launch a product "in house" like a big pharma company. There are many companies in the field that are specialized in this phase. Biotie could fund the launch of a product with call points focused on hospitals (a specialty field force) using outside services. However, if the product would be general practitioner based, we believe that the partnering is a better option for the company. Naturally none of Biotie's products are marketed directly to the consumer market, which would be a completely different marketing scenario. Biotie doesn't need to reach the end-consumer, the key is where and by whom they are prescribed. If this is more hospital based, the company can launch independently.

Biotie doesn't have to have the necessary resources to launch a product "in house". There are many companies in the field that are specialized in this phase.

It's also important to understand that the biotech companies can add value to the medicine without actually discovering anything "new". Generally this is done simply by collecting more data and therefore reducing the risks of further development. The sweet spot for this kind of activity is generally Phase 2, which is also the key area for Biotie. In general the company is focused in "value inflection points" like this.

One shouldn't think medicine development only in terms of "discovering" something new. Value can be added simply by collecting data and therefore reducing the risks.

The risk profile of a company is very much dependent on its focus areas. The later you are in the development process, the better the chances are that the product will actually be launched. Even though the risk of failure is reduced by focusing in the latter phases (higher probability of success), the amount of capital at risk in the latter phases is much larger, as the majority of R&D expenses will occur in Phase 3 (roughly 2/3 of the whole development process). Therefore there's always a certain balance of risk between different areas and the key aspect of Biotie's business is the risk management. In the new evolved strategy the risks of failures are lower, but if the company carries the financial risks of large Phase 3 studies by itself and doesn't use partners, possible negative surprises could have a significant financial impact.

There's often a tradeoff in biotech when it comes to risks: clinical risks mitigate when moving further in the pipeline, but at the same time the financial investments get higher.

1.2 Biotie's current product portfolio

Biotie's product portfolio currently consists of five medications in different development phases. The company also has an option to purchase one more. However, in the Q4 report Biotie said that it is not planning to use the option and won't be making further investments in the NRL-1 option. Therefore we have removed it from the current product portfolio.

Biotie's product portfolio currently consists of five medications in different development phases.

Biotie's products are still mostly in developing stages, mainly in clinical Phases 2 or 1. The only product that has been launched to the markets is Selincro, and we also believe it to be clearly the most valuable asset that company currently possesses. However, there's also definitely significant potential in tozadenant (for Parkinson's disease) and in SYN120 (for Alzheimer's disease), which the company is currently preparing for Phase 2 studies. When it comes to the value drivers, three of the above mentioned are clearly more important than the rest. Selincro, tozadenant and SYN120 hold more than 90 % of the value that we have established in Biotie.

The only product that has been launched to the markets in Selincro. We see significant potential in Tozadenant, which is currently a Phase 3-ready medicine for Parkinson's disease.

Nepicastat (for cocaine dependence) is currently an interesting opportunity due to its risk structure; NIDA is paying for the phase 2 studies. Therefore Biotie only has upside regarding this medicine. However, the end-market is very challenging and there's a high risk of failure, which naturally limits the value of nepicastat. The fifth drug BTT-1023 has finished Phase 1 studies and is a much longer term project than those mentioned above.

Also SYN120 for Alzheimer's disease would be very valuable if successful. Biotie currently prepares SYN120 for phase 2 studies.

We are focusing more in the pipeline that's in a more advantaged stage – these are the projects that are currently most important for the share price development. In the following graph 1 we have

presented Biotie's current product portfolio as well as their development phases and possible partners. Note that there's a more in-depth, detailed analysis of the different products in chapter 2.

Product	Phase 1	Phase 2	Phase 3	Launched	Partner
Selincro (nalmefene) *Alcohol dependence*					Lundbeck
Tozadenant (SYN115) *Parkinson's disease*			End-of-phase 2 meeting soon. Looking for new partner.	Launch could be in 2020	Needs to fina a new partner before P3.
SYN120 - *Alzheimer's disease and other cognitive disorders.*		Preparations for P2 have started			
Nepicastat (SYN117) - *Cocaine dependence*		Results expected 2015			
BTT-1023 (VAP-1 antibody) *Fibrosis*		Preparing for P2, but financing still unknown.			

Graph 1. *Biotie's current product portfolio.* *Source: Inderes, company materials*

Biotie's lead product is clearly Selincro, which was launched to the markets in 2013. Selincro (nalmefene) is an orally administered medicine for the treatment of alcohol dependence. Biotie has licensed the global development and commercialization rights to nalmefene to Lundbeck, a major company in CNS drug development and commercialization. Lundbeck has launched Selincro in 20 countries in Europe so far and is planning to launch it to further countries, including three key markets this year. There's a possibility for the Japanese markets as well, following the arrangement Lundbeck recently announced with Otsuka. Currently there are no announced plans to go to the US. While the market for alcohol dependency could be a very significant revenue generator for Biotie, it's a difficult market commercially. Selincro is a paradigm shifting drug, which means that there's a lot of work involved, including "teaching" the medical community to prescribe the drug to patients. After all, most treatments for alcohol dependence so far have been focused on abstinence and quitting drinking all together. Selincro is for reducing heavy drinking by reducing the urge to drink.

Tozadenant is currently waiting for the FDA meeting after completion of Phase 2 clinical studies. This end-of-phase 2 meeting is one of the key events in H1'14. There was a significant setback in the development of tozadenant recently, when Biotie's partner UCB decided to return the rights to tozadenant to Biotie. Biotie regaining the rights follows UCB's assessment of its early and late stage clinical development pipeline, as well as its preclinical opportunities. These do not reflect any concerns regarding the safety or efficacy of tozadenant. Tozadenant was originally licensed to UCB in 2010, and UCB paid Biotie 20 million dollars to exercise its license in February 2013. Soon after this the deal fell apart. While this creates a lot of uncertainty, it doesn't remove the huge potential that tozadenant has. However, now Biotie needs to find a new partner for tozadenant. The Phase 3 studies for a Parkinson's drug are going to be expensive (>100 MEUR), and even though Biotie has a solid financial position, it doesn't have adequate resources do this without a partner. Biotie expects to be able to give further guidance on any potential change in development timelines during Q2'14. Together with Selincro, tozadenant still builds the core of Biotie's portfolio.

SYN120 is phase 2-ready asset now, which means that it will take a long time before it could reach the markets. It is developed for Alzheimer's disease, which means that it also has huge potential. SYN120 has an interesting profile; it is a third generation 5-HT6 antagonist that has been designed to be devoid of some of the cardiovascular side effects that have impacted this class of drugs. However, it also has an additional mechanism of action. Beyond blocking the 5HT6 receptor, SYN120 will also antagonize 5HT2a receptors in the CNS. The latter mechanism of action has recently demonstrated encouraging efficacy in psychosis associated with Parkinson's disease. SYN120 would be a first in class drug combining these two factors, which makes it very interesting.

We believe that these three mentioned here hold over 90 % of the value of Biotie.

Biotie's lead product is clearly Selincro, which was launched to the markets in 2013. Selincro (nalmefene) is an orally administered medicine for the treatment of alcohol dependence.

Biotie has licensed global development and commercialization rights to nalmefene to Lundbeck. Lundbeck has launched Selincro in 20 countries in Europe so far and is planning to launch it further countries, including in three key markets, this year.

Selincro is a paradigm shifting drug; treatments for alcohol dependence so far have been focused on abstinence and quitting drinking all together. Selincro is made for reducing heavy drinking by reducing the urge to drink.

Tozadenant is currently waiting for the FDA end-of-phase 2 meeting, which is one of the key events in H1'14. There was a significant setback in the development of tozadenant recently, when Biotie's partner UCB decided to return the rights to tozadenant to Biotie. Now Biotie needs to find a new partner for tozadenant, which creates a lot of uncertainty. Together with Selincro, tozadenant still builds the core of Biotie's portfolio.

SYN120 is phase 2-ready now, so it will take a long time before it could reach the markets. However, it has a unique profile for Alzheimer's disease, which means that it also has a huge potential.

During the summer 2013 Biotie acquired an option to buy Neurelis and medicine called NRL-1, which has just completed the Phase 2 clinical studies. Biotie paid one million dollars in cash to Neurelis in June 2013 for the option to acquire Neurelis for a pre-determined price of 8.75 MUSD (in Biotie shares). However, Biotie decided not to exercise the option, quoting "timely access to market is not guaranteed". We believe that the reason behind this was a change in the competitive situation - there's probably a similar drug entering the market prior to the possible launch of NRL-1, so the potential wasn't adequate anymore. Biotie stated that it will not make any further significant investment into this opportunity until further notice. We believe that NRL-1 is buried for the time being, thus we have estimated its value to be zero at this point.

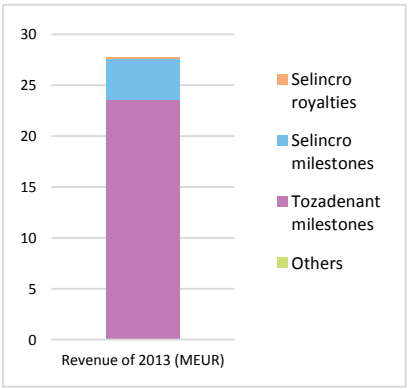
1.3 Biotie's earnings logic

The earnings logic for Biotie is very different from the traditional industrial models. It doesn't have steady net sales, but it generally has a relatively predictable cost base. It's critical to understand the basics of medicine development: the cost occurs before the sales. You have to invest in the development of a product first, and if successful, you'll be paid.

Biotie's main income streams are milestone payments and royalties from the sales of products. These can differ greatly from year to year.

Milestone payments and royalties

Biotie's main income streams are milestone payments, royalties from the sales of products (currently only Selincro has been launched) and other minor income. As an example, you can see the revenue distribution in 2013 in graph 3. These are not official figures, but should be relatively close to the correct ones. However, it's important to realize that these differ from year to year. The milestone payments are agreed upon with partners; typically they are tied to certain triggers in the development process, such as approval to move to the next phase, or launch to the market. After a product has been launched to the markets, the royalties begin. These can be very significant and naturally depend on the actual sales of the product.



Graph 3. *Different sources of income. Source: Inderes*

The milestone payments are agreed upon with partners. Typically they are tied to certain milestones in the development process such as approval to move to the next Phase or launch to the market. Generally few details are given about these contracts, so estimating milestone payments is difficult.

Once the medicine is launched to the markets, the royalties from the actual sales (typically through a partner) begin. Biotie's royalties are typically tiered with an average in the "mid-teens" or around 14-18 % of the sales. The further the company develops the medicine (and carries the risks) on its own, the higher the level of royalties will be. However, these are always a matter of contract and bargaining power. If the developed medicine were to become really successful, the value of royalties could be huge. Generally Biotie, as well as its peers, get around 5-10 years of "protected cash flow" before the patents or other product protection ends and generic copies enter the market. After the patents end, the royalties become quite insignificant if they continue at all (unless the product is extraordinary).

Once the medicine is launched to the markets, the royalties from the actual sales (typically through a partner) begin. Biotie's royalties are typically in the "mid-teens" or around 14-18 % of the sales.

There can also be other kinds of arrangements, e.g. shared R&D expenses with partners, though these aren't really net sales.

Balancing between different income streams is a part of risk management

The balance between different income streams is really difficult to estimate. There's always a balancing act with risk and reward for the company as well as its partners. The safer choice is to rely more on shared expenses or milestones related to the R&D costs, which limits both the downside as well as the upside. Shared expenses are paid whether there's ever actual income coming from the medicine. However, if the partner takes care of the expenses this would lower the amount of milestone payments and especially royalty percentage (all other factors being equal). On the other hand Biotie could carry all the development costs alone and even bring to product to the market without partners. Then no one would be sharing the cost load, but they wouldn't be sharing the profits either. As stated earlier, this business is in essence centered on risk management, and management has a huge role in determining the value of each investment.

There's always a balancing act with risk and reward when it comes to the different income streams. The biotech business is very much about the risk management and management has a huge role in determining the value of each investment.

Each of Biotie's products has its own risk/reward profile. These are somewhat challenging to determine, since the company naturally doesn't reveal all the details of its partnership contracts.

However, the persistently most difficult aspect to estimate is the risk of clinical development and the product profile. In general we would still say that the further along Biotie develops the products by itself, the higher the risk as well as the potential reward. Even though the clinical risk reduces as the development advances, the financial risk increases due to the elevating costs of achieving the next value inflection point. Without partnering Biotie would carry this risk on its own. Once again we could compare the situation to a start-up company; the further the company can develop its business without outside funding, the higher the potential reward, but also the higher the amount of "own capital" and risks.

Development projects are the "raw material" of biotechnology

It's also important to understand that the products in the pipeline are kind of like "raw materials" for Biotie (more specifically their IPR). Before the launch, their value is based solely on the sales potential. The development work that Biotie mostly does isn't really about discovering anything new, it's mostly about accumulating data. If this data is positive, meaning that the medicine is proven out to be effective, safe and well-tolerated, the value increases. If there are problems, value decreases and might even evaporate. For example the product might not produce positive efficacy data or dangerous side-effects are found. Especially between the different development phases, the company can use the "commodities" to trade in order to receive resources for another project or just gather cash if needed.

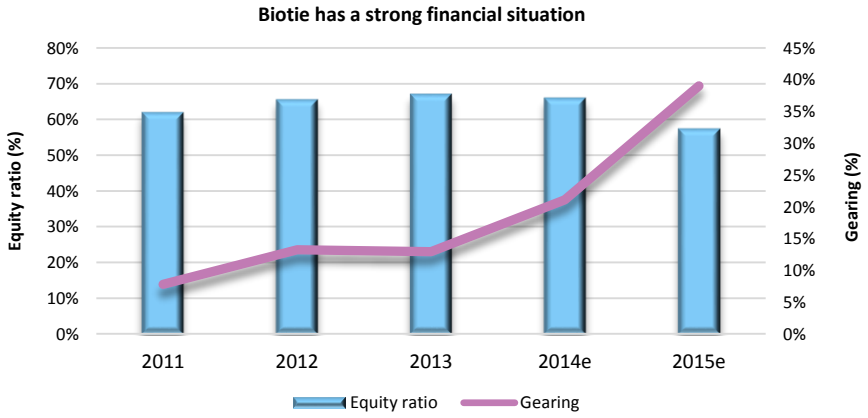
The products in the pipeline (their IPR) are "raw materials" in this business. Products with high potential and promising profile can have large value even if they are years away from creating any actual sales.

1.4 Financial position is solid

Biotie's financial position is currently solid. At the end of the year the company had roughly 44 MEUR of cash, which gives it a very comfortable buffer for the future. Biotie has also good prospects in milestone payments and reasonable royalties. We would say that the company's financial situation is very good compared to typical small biotech company in this business area. They would also have some "firepower" for acquisitions also, if there were suitable targets. However, we believe that the Phase 2 study of SYN120 will be the most significant investment for Biotie in the coming years.

Biotie's financial position is currently solid. At the end of the year the company has roughly 44 MEUR of cash, which gives it a very comfortable buffer for the future.

We believe that the Phase 2 study of SYN120 will be the most significant investment of Biotie in the coming years.



Graph 3. *Equity ratio and gearing of Biotie.* *Source: Inderes*

In the biotechnology sector the financial strength is often measured by cash burn rate. This basically measures the time that company can continue its current level of operations without new income (either equity or debt funding, or milestone payments). With 44 MEUR of cash, Biotie has plenty of time to work with. The company's annual costs are roughly at the level of 10 MEUR in FY'14, when considering internal projects that do not have an outside financing, as well as G&A costs.

In the biotech sector the financial strength is often measured by cash burn rate. Biotie's cash burn rate is currently relatively low, so Biotie has plenty of time to work with.

However, Biotie has decided to fund the SYN120 Phase 2 trials, which will increase the cash burn next year. When the costs of these P2 studies really start to accumulate in FY'15, the financial position could change significantly without new income. The Phase 2 studies could cost >10 MEUR annually, which will increase the cost base significantly. Biotie can carry them without problems, but there isn't much additional cash if the overall investment to SYN120 will be around 25-30 MEUR in the next few

The situation will change in 2015, when the SYN120 P2 studies will really start to accumulate costs. The Phase

years. A lot depends on the partnering of tozadenant; Biotie's financial position isn't strong enough to carry the costs of a Phase 3 study for it. We are assuming that Biotie will find a partner for tozadenant.

Biotie has also kept the option open to also progress with VAP-1, but we find It unlikely they would make significant investments in the project. The nepicastat development project is financed by NIDA, so it doesn't influence the cash burn rate.

All in all, Biotie's financial situation is solid and the financial "survival" isn't tied to any shortly upcoming milestone payments or royalties. We believe that the actual cash burn rate is relatively low in 2014, though the cash balance should be somewhat lower at the end of 2014 than it was at the end of 2013. After this the situation changes, but new information is likely to arrive prior to the end of 2014 (partnering of tozadenant).

There are many companies in the biotech sector who are going from milestone to milestone without any additional funds or room for error. Often these companies only have one product under development. In these cases it could be said that they are actually projects, not really long-term businesses. In case of negative data from one of the phases and failing to get the next milestone payments, the whole business is also often run down. Compared to these kinds of companies, Biotie's risk profile is almost non-existing, though still high in absolute terms.

2 studies could cost >10 MEUR annually, which will increase the cost base significantly.

We are assuming that Biotie will look for a partner for tozadenant. We aren't expecting significant investments to VAP-1 either. The nepicastat development project is financed by NIDA, so it doesn't influence the cash burn rate.

No distributable earnings, but also practically no interest-bearing debt

The shareholders' equity of the group amounted to 80.8 MEUR at the end of 2013. This means that Biotie's equity ratio was 69.2 % (FY'12: 66.7 %). However, the company's retained earnings were roughly 126 MEUR in the red at the end of the year, which means that investors shouldn't be expecting dividends any time soon. Biotie couldn't legally pay dividends even if it wanted, because it has accumulated losses to account for in the past.

However, we must point out that this is normal in the biotech industry: you have to develop the products before income occurs, and because this is very expensive, companies will have significant losses prior to launches even if the projects are successful. Biotie made its first positive net result in 2013, but it has plenty of losses from the prior years.

The historical losses aren't really a negative factor for investors coming in now. Actually, there are some clearly positive factors: 1) Biotie won't have to pay taxes in the coming years and 2) the company doesn't have to pay back capital loans from Tekes for a long time. The Tekes non-convertible loans have interest and capital that are only repayable if the company has sufficient funds within the group as a whole for profit distribution, which would mean that they become payable only after Biotie has made roughly 90 MEUR of net earnings. Even in the best case scenario, this would take years. At the end of 2013 Biotie's balance sheet had 16.3 MEUR of non-convertible capital loans from Tekes as well as 2.7 MEUR of long-term R&D loans from Tekes. In addition it had convertible capital loans amounting to 1.7 MEUR, but in general we could say that company has practically no net interest-bearing debt to burden its financials.

While the balance sheet is currently strong, Biotie's retained earnings are heavily in the red. Biotie couldn't legally pay dividends even if it wanted due to large historical losses. This is normal in the field: companies will have significant losses prior to launches. Biotie made its first positive net result in 2013.

The positive side is that Biotie won't have to pay taxes in the coming years and it doesn't have to pay back capital loans from Tekes for a very long time. In general we could say that the company has practically no net interest-bearing debt to burden its financials.

Biotechnology is an IPR business, so there are plenty of intangible assets

One thing that we still need to point out from the balance sheet is the amount of intangible assets and goodwill. At the end of 2013 company had 69.2 MEUR of intangible assets (FY'12: 71.1 MEUR) and 5.3 MEUR of goodwill (FY'12: 5.5 MEUR) in its balance sheet. These intangible assets and goodwill are tested for impairment annually, and whenever there is an indication that an asset may be impaired. It's completely normal that a biotech company has a significant amount of intangible rights on the balance sheet, after all the whole business is about these rights. Still, if Biotie were to be required to recognize impairments, it could have a material negative effect on the results and balance sheet, although they would not have a cash flow effect.

It's normal that a biotech company has a significant amount of intangible rights on the balance sheet, because the business is about the IPR. Still, if it should be required to recognize impairment in these assets, it could make a dent on the balance sheet.

1.5 Management has a critical role in the biotech industry

The management of any company is very important for its success, but it's crucial in biotech. When it comes to the job of the management, we could align biotechnology with an investment company that focuses on start-up companies. You are investing large sums of money either in already existing products in your portfolio, making acquisitions to widen your portfolio or divesting products in order to reduce risks or cut your losses. All these decisions have to be made with an analysis of the potential rewards, risks and the expertise and resources of the group. Because development projects are very expensive and their outcome is always uncertain, the risk management is a key part of the management duties. Still the company must take significant, justifiable risks when there's an intriguing opportunity available.

Most of the decisions are also "binary" with no middle way. Whether the company makes an acquisition or not (buy option could be "middle way") or makes a 100 MEUR investment in the phase 3 trial of a product or divests it (partnering could be a middle way, but not always on the table). These are the kinds of decisions that the management has to get right for the majority of the time in order to create value. The management is always in charge of capital allocation, but in biotech it's the determining factor whether the company is successful or not – just like in investing. Since the odds and the stakes are somewhat similar compared to start-up investing, we could argue that a good leader of a biotech company is similar to a successful investment manager – and naturally has to be equipped with an excellent knowledge of the pharmaceuticals industry.

The board of the company is also very important when it comes to Biotie. The majority of significant decisions made could be considered to be investment decisions. For instance, should they progress to the next phase of development and invest large sums of money in R&D, or to make an acquisition or a divestment, or enter a partnering contract? Most of these decisions are made by the board; its significance is larger than on average.

Management team and the board of Biotie

Both Biotie's management team and board have a very long experience in the field as well as the necessary expertise. President and CEO Timo Veromaa has been with the company since 1998 and the CEO since 2005. Everyone in the management team has a long experience in the field and there's plenty of more in the Board of Directors. William M. Burns was elected as the Chairman of the Board in the AGM on 3rd of April.

Management Team	Board of Directors
President and CEO: Timo Veromaa Biotie since 1998, CEO since 2005. Formerly Medical Director, Schering AG, Medical Director 1996–1998. Collagen Corporation, research and program manager 1994–1996. Stanford University, Postdoc Fellow 1990–1993.	**Chairman: William M. Burns** Chairman of the Board since April 3, 2014. Principal occupation: Member of the Board of Directors Roche and Shire PLC. Eearlier Roche from 1986 to 2010, most recently as Chief Executive Officer of the Division of Roche Pharmaceuticals.
CMO: Steve Bandak, M.D. Formerly Synosia CMO; more than 25 years' experience at Lilly	**Merja Karhapää** Principal occupation: Chief Legal Officer (CLO, Group Legal Affairs) and Company Secretary(since 2008)
CFO: David Cook Formerly Jazz Pharma, EUSA Pharma, Zeneus Pharma, PricewaterhouseCoopers	**Bernd Kastler** Principal occupation: Company Director Employment history: Co-founder and from 2002 until 2008 CEO of elbion NV.
COO: Mehdi Paborji Formerly Theravida; Theravance; more than 15 years' experience at BMS	**Ismail Kola** Principal occupation: Executive Vice President of UCB Pharma and President of New MedicinesTM UCB Pharma
	Guido Magni Principal occupation: Managing Director of Versant Euro Ventures

Table 1. *Management Team and Board of Biotie.* *Source: Company materials*

The management of any company is very important for its success, but it's crucial in biotech. The management is always in charge of capital allocation, but in biotech it's the determining factor whether a company is successful or not.

We could argue that a good leader of a biotech company is similar to a successful investment manager – and naturally has to be equipped with an excellent knowledge of pharmaceuticals industry.

Also the board of the company is very important when it comes to Biotie. Major decisions are made by the board in biotech and therefore its significance is very large.

Both Biotie's management team and board have a very long experience in the field as well as the necessary expertise.

The track-record of Biotie isn't a huge success, but over the past years the development has been solid. Biotie has been able to get Selincro launched and there has been good progress in the other development projects also.

1.6 Ownership structure of Biotie

The ownership structure of Biotie is very interesting. The biggest owners include Lundbeck, the company's partner with Selincro, and the old tozadenant partner UCB. Especially the stake held by Lundbeck opens up interesting possibilities for speculation. We'll discuss this topic further in chapter 3.3. On the other hand, it's unclear how UCB sees its ownership in Biotie after it returned the rights to tozadenant to the company recently. It might be interested in divesting the shares, since pharmaceuticals generally do not have normal "financial investments" without other incentives. Therefore there's a possible 9 % stake hanging over the share; this could help explain the pushed down share price currently witnessed.

Biotie's biggest owner is Invesco with a 17 % share of the company. Invesco is a very large investment management company and listed on the NYSE (also a part of S&P500). Invesco, or more accurately one of its subsidies, become an owner of Biotie back in 2009 and was also one of the major institutions that took part in the share issue in 2012.

Most of the large positions of foreign institutions are held in the nominee register, so they are not in the official owners' lists updated every month. Therefore we don't know the exact ownerships of Invesco or UCB (~9 %), Lundbeck (~4 %), Versant (~8 %), Abingworth (~4 %) and Novo A/S (~3 %). A total of 51 % of shares are under the nominee register.

Biotie also has a large amount of Finnish retail investors as owners, they own about 23 % of Biotie. At the end of 2013, Biotie had 15 161 shareholders in total (2012: 13 253). Other than that there are mostly typical institutions for a Finnish company: Ilmarinen, Nordea, Pohjola, Sitra and Veritas with relatively small positions (around 2-4 %).

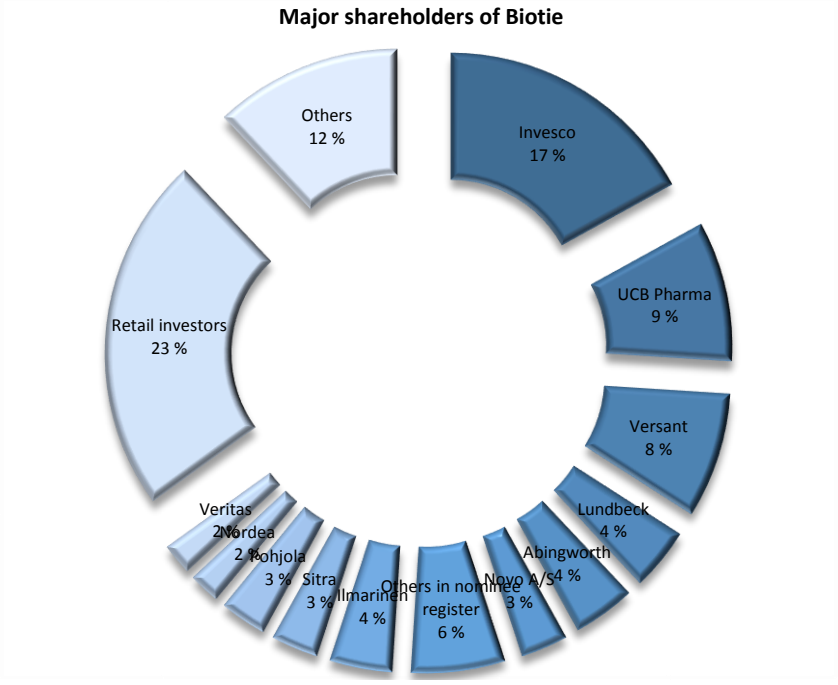
Overall, we would say that the shareholder structure doesn't exclude the company from a possible takeover attempt, if someone were to orchestrate one in the future. We believe that the significant owners would be willing to sell Biotie, if the price was right in their opinion. We aren't aware of any kind of "poison pills" either, so Biotie could potentially be a buyout target for a larger company in the future.

The ownership structure of Biotie is very interesting and gives room for different speculations on M&A.

Lundbeck is one of the biggest shareholders, and if Selincro is financially successful, it would also be one of the biggest sources of revenue for Biotie. Therefore it could make sense to buyout Biotie in the future.

Another question is what UCB is planning to do with its 9 % share of the company, now that it has returned the rights to tozadenant to Biotie. UCB might be interested in divesting the shares.

The shareholder structure doesn't prevent possible takeover attempts in the future. We aren't aware of any kind of "poison pills" either, so Biotie could potentially be a buyout target in the future.



Graph 4. *The shareholder structure of Biotie, dated January 2014.* *Source: Company material*

2. Detailed analysis of the product portfolio

Biotie's value is based on its product portfolio and the potential that it holds. In this chapter we open up the current situation of the key products. We also shortly cover prospects further down the development pipeline, with the main focus on those that are closer to the "value inflection points" (such as new research data, partnering decisions or sales of Selincro). These are the ones currently most critical considering the company's valuation.

Note that we have gathered some additional information on the products and on the markets in the appendix. Here we attempt to limit the massive amount of information specifically to those factors that we believe to be most critical in the eyes of investors.

Biotie's value is based on its product portfolio and the potential that it holds. We are focusing on those products close to the value inflection points, because these are critical for the share price development.

2.1 Biotie's spearhead product: Selincro

Biotie's lead product Selincro (nalmefene) is an orally administered opioid receptor ligand for the treatment of alcohol dependence. Selincro is approved in Europe for the reduction of alcohol consumption in adult patients with alcohol dependence who have a high level of alcohol consumption.

Selincro is taken on an 'as needed' basis to reduce the desire to drink, thus offering patients a novel treatment option compared to traditional methods, aimed at total abstinence and usually include intensive psychosocial therapy. Biotie has licensed the global development and commercialization rights to nalmefene to Lundbeck.

Excessive alcohol consumption is common in many parts of the world, especially in Europe where more than 14 million people are alcohol dependent. WHO (World Health Organization) has estimated that 58 million Europeans consume alcohol at levels considered harmful or hazardous. No one can deny the significant negative effects of excessive alcohol consumption, and it has been estimated that 25% of emergency room admissions are directly alcohol related. Further, 10 % of deaths in the Western world are alcohol related. It's almost impossible to estimate the financial burden caused by excessive alcohol consumption. However, it has to be massive when considering the direct costs (burdening the healthcare system) as well as indirect costs (such as lower level of efficiency and unemployment).

Even though no one disputes the negative effects, very few are receiving treatment for alcohol dependency. In Europe the treatment gap is very large, with only 8 % of patients receiving any treatment. Both abstinence and reduction goals should be considered as part of a comprehensive treatment approach for patients with alcohol dependence in Europe.

Selincro Nalmefen

Biotie's lead product Selincro (nalmefene) is an orally administered opioid receptor ligand for the treatment of alcohol dependence. Selincro is approved in Europe for the reduction of alcohol consumption in adult patients with alcohol dependence.

It is estimated that more than 14 million people in Europe are alcohol dependent; a great deal drink at levels considered harmful or hazardous.

While there's a large amount of people that have alcohol dependence, very few are receiving treatment for it. In Europe the treatment gap is very large, with only 8 % of patients receiving any treatment.

Selincro helps to control and limit the intake of alcohol. Basically Selincro should remove a person's desire to drink by blocking the good feeling of "being drunk".

Selincro is to be taken as-needed; on each day the patient perceives a risk of drinking alcohol, one tablet should be taken.

How does Selincro work?

Selincro is a small molecule opioid receptor modulator that inhibits the reward pathway in the brain that reinforces the desire and craving for alcohol and other addictive substances. Unlike existing therapies, treatment with Selincro is not aimed at keeping the patients from drinking altogether. Instead, Selincro helps to control and limit the intake of alcohol. In layman's terms, Selincro should remove a person's desire to drink by blocking the good feeling of "being drunk".

Selincro is targeted for the reduction of alcohol consumption in adult patients with alcohol dependence, who have a high drinking risk level without physical withdrawal symptoms, and who do not require immediate detoxification. Selincro is to be taken as-needed; on each day that the patient perceives a risk of drinking alcohol, one tablet should be taken, preferably 1-2 hours prior to the anticipated time of drinking.

In the clinical studies patients treated with Selincro showed over 40% reduction in total alcohol consumption within the first month, and at the study's end (6 or 12 months) the alcohol intake was reduced in excess of 60 %. Data from the 1-year study suggested longer term efficacy of Selincro

beyond 6 months and up to 1 year of treatment. There were no major safety concerns identified during the studies, and Selincro was generally well tolerated.

In the clinical studies patients treated with Selincro showed more than 40 % reduction in total alcohol consumption within the first month, and at the study's end (6 or 12 months) the alcohol intake was reduced by more than 60 %. There were no major safety concerns identified during the studies and Selincro was generally well tolerated.

Picture 2. *The indicative results of Selincro's Phase 3 trials.* *Source: Company materials*

Biotie has licensed Selincro with Lundbeck

Biotie has licensed global development and commercialization rights to nalmefene to Danish CNS specialist, H. Lundbeck A/S (Lundbeck). Lundbeck has significant experience and a substantial track record in depression, a therapeutic area with many parallels to alcohol use disorders. Lundbeck's specialist marketing force and its long-established relationships with prescribers in the relevant therapeutic areas will be important in driving a successful launch, and maximizing the market potential for nalmefene.

Biotie has licensed global development and commercialization rights to nalmefene to Danish CNS specialist Lundbeck.

The alcohol dependence market has a large potential…

Although excessive alcohol consumption is a problem almost everywhere in the world, the treatment of alcohol dependence is somewhat different in different areas. In the United States the treatment is heavily focused on complete abstinence and there are only very few doctors (<20 %) who accept reduction of drinking as an acceptable treatment. In addition, the data protection available to Selincro is significantly weaker in the US, which may be the reason there have been no announced plans to launch Selincro in the US.

The main market of Selincro is Europe. In Europe both abstinence and reduction goals are considered acceptable and relevant components of a comprehensive treatment approach for patients with alcohol dependence. In February 2013 Lundbeck received European marketing authorization applying to all 27 European Union member states for Selincro. Lundbeck will provide Selincro as part of a new treatment concept that includes continuous psychosocial support focused on the reduction of alcohol consumption and treatment adherence.

Lundbeck launched Selincro in the first European markets in April 2013, and by September 2013, it was available to alcohol dependent patients in Norway, Finland, Poland, Estonia, Latvia, Lithuania, Portugal, Iceland, Sweden, the UK, Bulgaria, the Czech Republic, Hungary, Slovenia, Italy, the Netherlands and Denmark. Lundbeck will continue the rollout of Selincro in Europe through 2013 and into 2014. In addition there are clear plans to also launch Selincro in Japan, which would be another significant market. So far we haven't taken the opportunity of Japan into our analysis, as we see at mostly as an interesting "option" that comes with Biotie.

We would estimate that those with really serious problems with alcohol are not potential target group for Selincro. Those with severe alcoholism might be too far gone for a drug that requires

The main market of Selincro is Europe and Lundbeck launched Selincro in the first European markets in April 2013. In Europe both abstinence and reduction goals are considered acceptable treatment approaches for patients with alcohol dependence. In the US the treatment is heavily focused on complete abstinence, which makes it a difficult market for Selincro.

There's also a large market potential in Japan. Currently we see this as mostly an interesting "option" that comes with Biotie.

Those with really serious problems with alcohol are not the potential target group for Selincro. This limits the

anticipation and self-control. This limits the market somewhat to those who have significant amounts of heavy drinking days (HDDs), but still function and work normally without drinking.

In addition there is a huge amount of people that are so called "risk users" of alcohol, and this would be the key target group for Selincro in our eyes. Overall, the market potential of Selincro is large, especially when thinking from Biotie's perspective.

market to those who have significant amount of heavy drinking days but still function "normally". In addition there is a huge amount of "risk users" that could find Selincro useful.

…but it is also commercially challenging

Unfortunately the large potential doesn't automatically mean large commercial success. Selincro represents a paradigm shift in treating alcohol dependency – a reduction in drinking as opposed to complete abstinence. This approach, which is empowering for patients, is needed in light of the low treatment rates under the current abstinence strategy. This is also increasingly being recognized. However, the alcohol dependence market is still very much undeveloped, mostly as a result of inadequate therapies, so the breakthrough will definitely require a lot of work.

It is estimated that only 15 % of those suffering from alcohol dependence are diagnosed and significantly less are currently receiving any medicines. This is partly because alcoholism as a disease has a "bad reputation" (patients are considered to be failures by others) and partly because there haven't been any suitable medication available (with no treatment, it can be ignored by doctors). Since Selincro is bringing a new solution to the markets, it will have to create a market for itself. This will take both time and money, and of course the success isn't guaranteed (note that these costs will be carried by Lundbeck). We believe there will be a requirement to change the perception of the disorder from one requiring psychosocial treatment to one being drug treatable.

The alcohol dependence market is undeveloped mostly as a result of inadequate therapies, so the breakthrough of a paradigm shifting drug like Selincro will require a lot of work.

It is estimated that only 15 % of those suffering from alcohol dependence are diagnosed and significantly less are receiving any medication.

Competitive situation should be favorable

While Selincro is a novel medicine for the reduction of drinking, it isn't completely without competitors. Oral naltrexone (available as Revia and several generics) has been approved since the 1990's for the treatment of alcohol dependence in the US and some European markets, but has not been a commercial success. More recently, an injectable depot formulation of naltrexone, Vivitrol from Alkermes, was approved in the US for the treatment of alcohol dependence in patients who are able to abstain from alcohol. The sales of Vivitrol have been disappointing, though it's important to understand that there was a requirement for abstinence prior to commencing therapy, and monthly injections thereafter that are significant barriers to treatment. It wasn't a success either treatment wise, since 75 % of patients relapsed during the first year of treatment.

There are also other medicines that target complete abstinence. Probably the most well-known is Antabuse (or Antabus). It blocks the processing of alcohol in the body by inhibiting acetaldehyde dehydrogenase, thus causing an unpleasant reaction when alcohol is consumed. Basically patients cannot drink any alcohol without feeling nauseated. Therefore enjoying any alcohol is basically impossible when using these drugs, so reduction of drinking isn't an option. Campral is also a drug used for treating alcohol dependence. Campral's active substance acamprosate is thought to stabilize the chemical balance in the brain that would otherwise be disrupted by alcoholism, possibly by antagonizing glutamatergic N-methyl-D-aspartate receptors (NMDA) and agonizing gamma-aminobutyric acid (GABA) type A receptors. Campral was manufactured and marketed in the US by Forest Laboratories until it became generic, while Merck KGaA markets it outside the US. Reports indicate that acamprosate only works with a combination of attending support groups and abstinence from alcohol. For reduction of drinking Selincro is currently the only valid choice.

There shouldn't be similar drugs entering the market in the next few years. According to Biotie, there are a few competitive products in development. Amongst these, Alkermes has samidorphan (ALKS-33), an oral opioid receptor modulator. It has finished Phase 2 clinical trials, but it hasn't moved forward to Phase 3, and might be shifting focus away from alcoholism. It would have probably been the most significant competitor for Selincro, so this possible shift is very interesting.

Natural Pharmacia International (NPI) has studied the power of certain extracts of the kudzu plant in reducing alcohol drinking. Puerarin, a 5-HT2c receptor antagonist and GABA receptor antagonist, is a result of these studies. NPI has funded a Phase 2 clinical trial conducted at Mclean Hospital to

Selincro is a novel medicine for the reduction of drinking, but there are still competitors. So far the success of these treatments has been very poor, which also raises uncertainty concerning Selincro's sales expectations.

The most well-known "competitor" is Antabus, which blocks the processing of alcohol in the body by inhibiting acetaldehyde dehydrogenase, thus causing an unpleasant reaction when alcohol is consumed. This drug is naturally targeted for complete abstinence.

There are some competitors also in the pipeline, but nothing that would have a clearly better profile or that would be coming to the market during the next few years.

Perhaps the most relevant competitor in the pipeline

validate the hypothesis that short-term treatment with this compound will reduce alcohol self-administration in a simulated natural settings. While there has been some activity, no major trials should be in progress right now.

Just to mention few others in the pipeline, Omeros has a Phase 2-ready PPAR agonist. In addition ADial Pharmaceuticals has a low dose ondansetron and an ondansetron and topiramate fixed dose combination in Phase 2. The same company also has AD04 (serotonin-3 antagonist) that is being developed as a treatment for alcohol use disorder in patients of select genotypes. It might be progressing to Phase 3 soon, but has a more limited target group and probably isn't going to be a major competitor for Selincro. The National Institute on Alcohol Abuse and Alcoholism has an NK1 receptor antagonist approved as an antiemetic called aprepitant in Phase 2 for alcohol dependence. There hasn't been progress in a long time, so it might be buried already.

was samidorphan (Alkermes), but it hasn't moved forward to Phase 3, and might be shifting focus away from alcoholism.

In general the competitive situation shouldn't be a major factor in the success of Selincro; the key is the acceptance among doctors and patients.

Class	Main brands	Timeline	Efficacy / relevancy	Manufacturer
In the market				
Disulfiram	Antabuse / Antabus	Very old	Patients cannot drink alcohol without feeling nauseated	Barr/Sanofi
Naltrexone (oral)	ReVia	1994	Naltrexone's mechanism of action in alcohol dependence is not fully understood. Success has been relatively modest.	Barr Labs
Naltrexone (depot injection)	Vivitrol	1994	Requirement for abstinence prior to commencing therapy; monthly injections	Alkermes
Acamprosate	Campral	1989 / 2004	Had been found to be relatively efficacious, but specific role in alcoholism treatment remains to be more clearly defined.	Merck Serono/Forest
In the development pipeline				
samidorphan		Phase 2-ready	Has finished Phase 2 clinical trials, but might now be shifting focus away from alcoholism.	Alkermes
Puerarin		Phase 2	No major trials should be in progress right now. We do not believe this to be a relevant competitor.	Natural Pharmacia International
PPAR agonist		Phase 2-ready	Reseearched for the treatment and prevention of addiction to substances of abuse (e.g. opioids, nicotine and alcohol)	Omeros
ondansetron / topiramate, more recently serotonin-3 antagonist (AD04)		Phase 2	The Phase 3 trial to test AD04 for the treatment of alcohol in patients with the targeted genotypes is expected to commence in early 2014.	ADial Pharmaceuticals
Aprepitant		Status unknown	Most likely the development for alcohol dependency has been discontinued.	Merck

Table 2. *Drugs for alcohol dependency.* *Source: Company information, Inderes*

All of these development products are several years from potential registration filings. Therefore the competitive situation shouldn't be a major factor in the success of Selincro; the key is the acceptance among doctors (for reduction, not abstinence) and patients.

Another key factor is the favorable reimbursement decisions in the different markets, because without them the potential of Selincro is limited.

If the new treatment method is widely accepted by doctors and patients, and the administrators will make favorable reimbursement decisions (these are made separately in each European country), we believe Selincro will be very successful. The next important "milestones" are the reimbursement decisions coming from Europe – these are critical for the potential sales of Selincro.

Financial estimates for Selincro

On short-term Selincro will be a key driver for Biotie's earnings. Under the terms of the agreement with Lundbeck, Biotie is eligible for up to 89 MEUR in upfront and milestone payments plus royalties from sales. A significant portion of this maximum amount of milestone payments is very unlikely to be reached, but the company got 4 MEUR of milestone payments in 2013 and should be receiving an additional 6 MEUR in 2014, once Selincro is launched in Germany, France and Spain.

Biotie should be receiving milestone payments worth 6 MEUR in 2014, once Selincro is launched in Germany, France and Spain.

Nalmefene (originally known as nalmetrene) was developed in the early 1970s and investigated for a wide variety of disease conditions. In the 1990's, it was approved in the US as an injectable treatment for the management of opioid overdose. Biotie and subsequently Lundbeck developed it for the treatment of alcohol dependence, and it has also been investigated for the treatment of other addictions such as pathological gambling. The protracted development timeline means that Biotie doesn't have valid composition of matter patents for it. However, nalmefene is expected to have market exclusivity in the EU via data protection for 10 years post launch, eliminating the risk of direct generic competition for that time period. Japan has a similar system, making it also a potential market and Lundbeck has already made a licensing deal with a Japanese partner Otsuka. This supports the case that there's significant potential for Selincro also in Japan. Before this Selincro needs to make its breakthrough in order to reach its potential.

Typically peak sales of medicine are reached in roughly four years after launch. Since Selincro is a paradigm shifting drug, its progress will most likely be slower. We believe it will take around seven years before the drug reaches its peak sales. Of course a lot depends on the investments and success of Lundbeck promoting Selincro. At least it currently seems like they believe in the drug strongly, and are ready to put significant resources behind it.

The royalties from Selincro should also be a significant contributor to the earnings. They are naturally based on the sales of Selincro both in Europe and possible later in Japan, where the royalties of Biotie will be lower (single digit). We believe that the size of the potential market in Europe is around a billion euros or 15 million people. However, this market has to be reached first. Selincro should have a possibility to reach a market share of 33 % according to our estimates – in a positive scenario this could be much higher. If every person using Selincro would take 145 pills yearly, this would mean average annual sales of 450 euros per user annually. These are estimates by Lundbeck and based on the data from the development phases, as well as estimated pricing (3 euros per pill, wholesale price, price for consumers is naturally higher).

Main assumption behind our Selincro estimates (base case)	
Estimated alcohol dependent population in EU	Around 15m, but possible even 50m considering the nature of the dependency
Diagnosis rate (%)	15 % (current) increasing to 30% (at peak)
Diagnosed patients	2.3m (current) increasing to 4.5m (at peak)
Drug treatment rate %	8 % (current) increasing to 15% (at peak)
Patients receiving drugs	1.2m (current) increasing to 2.25m (at peak)
Selincro market penetration	Slowly increasing and peaking at 33 % by 2021
Patients using Selincro	Around 740 000 / year at peak
Effective annual cost / patient	450 € (1 pill/2.5 days = 145 days at 3 € per pill, Lundbeck est.) - possible slides down over time
Peak annual sales	300 MEUR
Royalty rate %	15% is our estimate, should be between 13-17 %
Peak annual royalties	45 MEUR
Milestones (MEUR)	28 MEUR are still expected to be realized (Max. 89 MEUR)
Used WACC in discounting	16 %, which includes a significant risk premium
Terminal value	After the IPR protection ends, we are estimating very little cash flow

Exhibit 1. *Summary of assumptions to model Selincro forecasts* *Source: Inderes*

Our peak sales forecast for Selincro is 300 MEUR in Europe, which is below that of Lundbeck (roughly 340 MEUR), and we are also expecting a relatively slow market penetration. In our current model, Selincro reaches its peak sales in roughly seven years. Both these modest estimates reflect our view of the commercial challenge of Selincro. We believe it is sensible to wait for evidence on sales prior to upgrading our peak sales estimate closer to that of Lundbeck, since even reaching our estimates requires a successful launch for all the key markets. We will be much the wiser in a few years, when the launch has been made in Germany, France and Spain and we'll know the reimbursement decisions of major markets (including the UK).

Reimbursement decisions are critical to success, because costs of Selincro are relatively high (450 EUR annually per patient) and many patients might not be willing to use this kind of money. At least the market penetration will suffer significantly, if there are negative reimbursement decisions in the key markets.

Nalmefene was developed in the early 1970s for different purposes, which means that Biotie doesn't have valid composition of matter patents for it. However, nalmefene is expected to have market exclusivity in the EU via data protection for 10 years post launch, eliminating the risk of direct generic competition for that time period.

Typically peak sales of a medicine are reached roughly four years after launch. Since Selincro is a paradigm shifting drug that we discussed about, its progress will most likely be slower. We believe it will take around seven years before the drug is at its peak sales.

We believe that the size of the potential market in Europe is around a billion euros or 15 million persons. Selincro should have a possibility to reach a market share of 33 %.

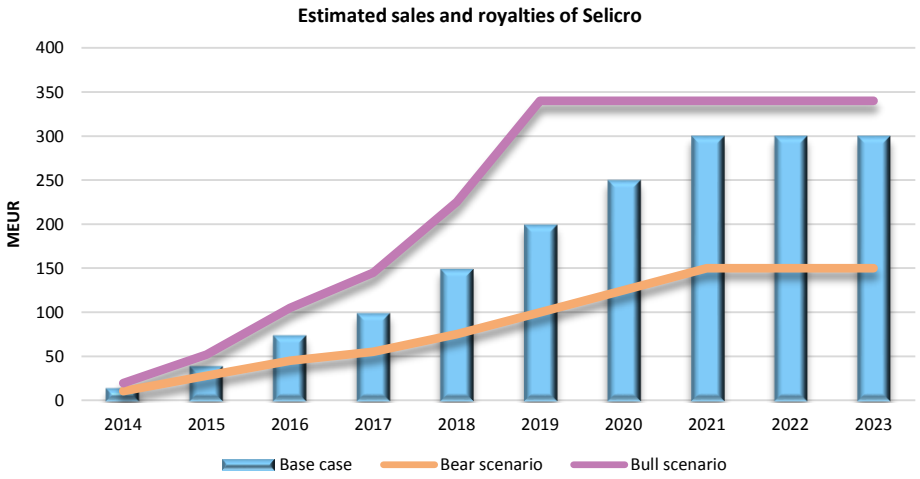
If every person using Selincro would take 145 pills in a year, this would mean average annual sales of 450 euros per user annually. These are estimates by Lundbeck.

Our peak sales forecast of 300 MEUR for sales of Selincro in Europe is below that of Lundbeck (roughly 340 MEUR) and also we are expecting a relatively slow penetration to the markets. Both are reflecting our view of the commercial challenge of alcohol dependency.

In the following graphs we have tried to demonstrate our expectations on the sales in Europe. There's a base case, which we have based our value on, as well as a positive bull scenario and a negative bear scenario. Since Selincro was just launched, there's naturally a high uncertainty on the sales development, but we are relatively sure that the actual sales will be within this range.

There's naturally a high uncertainty concerning its sales development. We also provided our base case, a positive bull scenario and a negative bear scenario in graph 5.

In our bull scenario Selincro reaches Lundbeck's estimate of peak sales (~340 MEUR) in 2019. This means that even our positive scenario is realistic, if Selincro is well received in all the major markets.



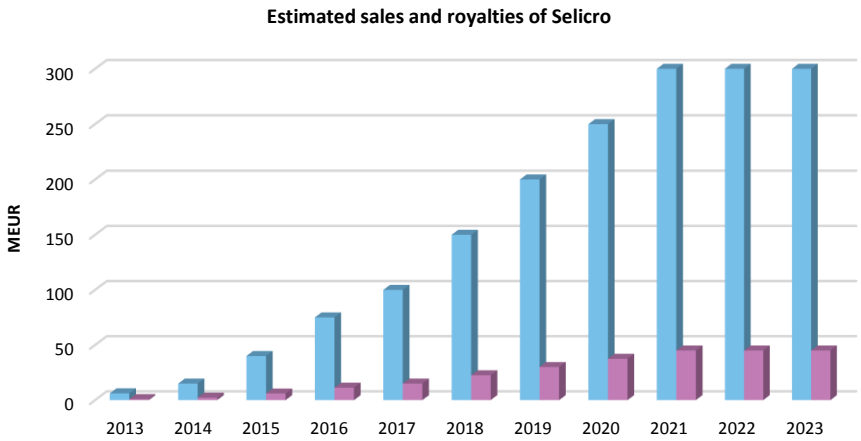
Graph 5. *Estimated sales of Selincro: base case, bear and bulls scenarios.* *Source: Inderes*

The company has said that the royalties are tiered with an average "in the mid-teens". In the case of Selincro we are using a royalty percent of 15 %, which Biotie receives directly from the sales of Lundbeck. This is close to the average and we believe it's a justified assumption that Biotie's role in developing Selincro was significant (thinking about the contributing of Lundbeck vs. Biotie), and the milestone payments were relatively low.

In the following graph we have also added the expected royalties to Biotie as the base case sales scenario. With the expected royalty rate of 15 %, Biotie's royalties would reach 45 MEUR with our peak sales estimate of 300 MEUR, thus meaning a massive jump in the current net sales of Biotie. Naturally this will take years even in a positive scenario.

The royalties from Selincro should be a significant contributor to Biotie's earnings. The company has said that the royalties are tiered with an average "in the mid-teens". In the case of Selincro we are using a royalty percent of 15 %.

With this royalty-% Biotie's royalties would reach 45 MEUR with our peak sales estimate of 300 MEUR.



Graph 6. *Estimated sales and Biotie's royalties from Selincro.* *Source: Inderes*

The value of Selincro (for Biotie)

Selincro has been successfully launched, so its probability of success is very high in clinical terms. There's a small amount of drugs that are pulled off markets after launch due to e.g. unexpected side-effects, but in clinical terms the probability of success is around 95 %. However, Selincro's commercial success is far from guaranteed. This is why we are using a 75 % probability for the commercial success of Selincro; this is our estimate of the probability that Selincro reaches at least the sales of our base case.

There should not be any significant expenses for Biotie deriving from Selincro, because the cost of goods sold is carried by Lundbeck. Also the financial risk is no longer relevant, since all the investments allocated to Biotie have already been made.

Based on these assumptions, we believe the financial value of Selincro to be around 87 MEUR. This calculation is based on risk-adjusted net present value (rNPV). Roughly 73 MEUR of this value derives from the expected royalties and the rest from the expected milestone payments that are still expected to come. The value of Selincro is very significant for Biotie - if our estimates are correct, Selincro's value is around 70 % of Biotie Group's current market value.

Value of Selincro	
Status	Approved and launched in EU
Probability of success (%)	75 % regarding commercial success
Estimated peak market share	33 %
Estimated royalty	15 %
Estimated peak sales	300 MEUR
Patent expiry	2023
Estimated value (rNPV)	87 MEUR

2.2 Tozadenant (SYN115) – Phase 2 ready

Tozadenant (SYN115) is a novel product for Parkinson´s disease. The product has a unique mechanism of action and, if the development project that is currently moving into Phase 3 is successful, it could represent the first new treatment modality for this disease in more than 20 years. There is currently a huge unmet need for PD disease-modifying treatments that slow progression or have neuroprotective properties.

The Phase 2 data of tozadenant has been promising, and the drug has a huge potential if it is successful in providing significant benefits to the patients compared to the current offering. However, recently the development of tozadenant suffered a significant setback. UCB decided to return global rights to tozadenant to Biotie. Biotie regaining the rights follows UCB's assessment of its clinical development pipeline, and does not reflect any concerns regarding safety or the efficacy of tozadenant. The decision left Biotie without a partner at a difficult time, since UCB was committed to funding the extensive Phase 3 studies. Biotie doesn't have the resources to fund the Phase 3 studies (that cost >100 MEUR) without a partner, so in order to progress without significant delays the company should find a new partner in the near future.

UCB's decision doesn't remove the undeniable potential of tozadenant, but it adds a significant risk related to partnering agreements. We believe that tozadenant is an intriguing asset for many companies in the field, but the terms of the agreement (such as up-front payments, milestones and royalties) might not be favorable for Biotie, if there isn't great demand for the product by multiple parties. This uncertainty effects heavily on the value that we are willing to give for tozadenant at this point, even though we realize the huge potential that it could have.

Tozadenant (SYN115) is a novel product for Parkinson´s disease. The product has a unique mechanism of action and could be a first-in-class inhibitor of the adenosine 2a (A2a) receptor.

The Phase 2 data of tozadenant has been promising and the drug has a very substantial potential; the PD market is huge.

Recently the development of tozadenant suffered a significant setback, because UCB decided to return global rights to tozadenant to Biotie. Now Biotie is forced to find a new partner before the P3 studies start.

About Parkinson's disease (PD)

Parkinson's disease is a progressive neurodegenerative condition. As the disease progresses the patients have difficulty walking, talking and completing simple daily tasks. Eventually patients are restricted to a bed or a chair and require constant nursing care. Overall prevalence of PD is estimated at 0.3 % of the general population (5,12) increasing to 1-1.2 % of those over 60 years of age (2,5,12). In the US there were an estimated 630 000 diagnosed PD cases in 2010, projected to rise to 1.34 million by 2040 (2). Mean age of diagnosis of PD is 62 years, and patient progression from first diagnosis to H&Y scale 5 generally takes 12-14 years (3,7). Around 15 % of PD patients are confined to nursing homes, and PD patients constitute over 9 % of the nursing home population between the ages 75-84 (2).

PD-related dementia has a prevalence of 0.2-0.5 % of the general population aged >65 years (1). Some 30-60 % of PD patients will develop psychosis over the course of their disease progression (4,6,8). PD-psychosis is associated with prolonged disease duration and the use of dopamine agonist therapy, but even in early PD (H&Y<2, duration <4 years) PD-psychosis may be detected in 3-8 % of patients (4).

Parkinson's disease (PD) is a progressive neuro-degenerative condition. As the disease progresses the patients have difficulty walking, talking and completing daily tasks.

Overall prevalence of PD is estimated at 0.3 % of the general population increasing to 1-1.2 % of those over 60 years of age. Some 30-60 % of PD patients will develop psychosis over the course of their disease progression.

Treatment of PD

There are currently no available therapies that are capable of curing Parkinson's disease and the market is dominated by symptomatic treatments targeting functional impairment in PD. This means that the goal of therapy is to reduce symptoms to allow patients to perform usual daily activities. Levodopa (L-Dopa) has remained the gold standard treatment for almost 40 years. Other existing therapies include dopamine agonists and the dopamine extenders. All these have limited efficacy, are associated with significant side effects (including dyskinesias, or sudden jerking movements) and their effects diminish over time, leaving patients with re-emergence of symptoms before their next dose ('wearing off'). Wearing off basically means that the time during which the drug (levodopa) is effective becomes shorter over time.

L-dopa remains the mainstay of drug therapy, with 85 % of US patients receiving L-dopa either as monotherapy or in combination (9). In general, physicians prefer to delay the onset of L-dopa therapy wherever possible because of fears of an overall eventual worsening of disease. Use of the MAO-

There are currently no available therapies that are capable of curing Parkinson's disease and so the goal of therapy is to reduce symptoms.

L-dopa remains the mainstay of drug therapy, with 85 % of US patients receiving L-dopa either as monotherapy or in combination. However, L-Dopa has a limited efficacy and significant side effects,

inhibitor Rasagiline has been associated with a delay in onset of L-dopa therapy and reduction in overall patients costs by 18 % in a 5 year period (10).

New therapeutic modalities that improve control of motor symptoms, delay the time to use of L-Dopa, reduce troublesome side effects, treat some of the non-motor symptoms such as dementia, depression, sleep disorders, and which slow progression of the disease are needed and will drive market growth. Because there are no available therapies that are capable of curing the disease, the current goal of therapy is to reduce the symptoms to allow patients to perform usual activities and to balance the benefits against the side effects.

A review of the competitive landscape shows around 60 new compounds currently in development for PD (discounting new formulations of existing therapies). Of these, around 20 would be considered as symptomatic therapies targeting the same patient segment as the Biotie molecule SYN115. Considering only those compounds in advanced development (clinical Phase 2 or beyond) the competitor landscape amounts to 14 molecules, and under standard attrition rates we anticipate 2-3 would complete development and launch around the same time as SYN115. (Source Thompson-Rueters Cortellis pipeline analysis)

e.g. "wearing off". Many new drugs like SYN115 are in the development pipeline to reduce the side-effects.

Roughly 60 new compounds are currently in development for PD, of which around 20 could be considered symptomatic therapies targeting the same patient segment as the SYN115.

Infobox - What is Parkinson's Disease (PD)?

Parkinson's disease (PD) is a chronic and progressive movement disorder, meaning that symptoms continue and worsen over time. The cause is unknown, and although there is presently no cure, there are treatment options such as medication and surgery to manage its symptoms. Parkinson's involves the malfunction and death of vital nerve cells in the brain, called neurons. Parkinson's primarily affects neurons in the area of the brain called the substantia nigra. Some of these dying neurons produce dopamine, a chemical that sends messages to the part of the brain that controls movement and coordination. The non-motor symptoms experienced by Parkinson's patients are likely secondary to the underlying loss of dopaminergic neurons and potentially other types of neurons. As PD progresses, the amount of dopamine produced in the brain decreases, leaving a person unable to control movement normally.

The specific group of symptoms that an individual experiences varies from person to person. Primary motor signs of Parkinson's disease include the following:

- tremor of the hands, arms, legs, jaw and face
- bradykinesia or slowness of movement
- rigidity or stiffness of the limbs and trunk
- postural instability or impaired balance and coordination

Scientists are also exploring the idea that loss of cells in other areas of the brain and body contribute to Parkinson's. For example, researchers have discovered that the hallmark sign of Parkinson's disease - clumps of a protein alpha-synuclein, which are also called Lewy Bodies - are found not only in the mid-brain but also in the brain stem and the olfactory bulb.

These areas of the brain correlate to nonmotor functions such as sense of smell and sleep regulation. The presence of Lewy bodies in these areas could explain the nonmotor symptoms experienced by some people with PD before any motor sign of the disease appears. The intestines also have dopamine cells that degenerate in Parkinson's, and this may be important in the gastrointestinal symptoms that are part of the disease.

Who is affected by Parkinson's disease?
Although it affects both men and women statistically, men have a slightly higher chance of developing the disease. The risk of developing Parkinson's disease also increases with age, with the average age of onset being 65 years old. Five to ten per cent of people who develop it are under 40 years old. When symptoms appear in people aged 21-40, this is known as young-onset Parkinson's disease and in under 18 year olds, juvenile Parkinson's disease although this is extremely rare. No one knows exactly why people get Parkinson's disease, but viral infection or environmental toxins may play a part. People with a parent, sibling or child with Parkinson's disease, are twice as likely to get it as other people.

What are the stages of Parkinson's disease?
Parkinson's disease is often divided into two parts; early stage and advanced stage disease:

- Early stage: when symptoms appear and start to affect everyday activities, such as washing, getting dressed and walking, enough so that treatment is needed.
- Advanced stage: when motor (movement) complications occur, due to use of one of the main treatments for Parkinson's disease, levodopa. These complications usually happen when someone has been taking levodopa for some time.

The prevalence of PD and the market opportunity

Parkinson's disease is one of the most common neurodegenerative disorders occurring with an incidence second only to that of Alzheimer's disease and a prevalence in the US, five major EU countries (5MEU) and Japan, of approximately 1.6 million. It is estimated that the prevalence is roughly 7-10 million globally.

The average age of onset is 60 years and, as the risk of developing Parkinson's disease increases with age, its prevalence is expected to increase as the global population ages. Especially the developed countries are relevant when it comes to the market potential. Prevalence is expected to double by 2050, which means that this market is growing steadily as the population ages. This will cause increasing economic and social burdens on society.

In 2010, the sales of Parkinson's drugs in the United States, 5MEU and Japan, were approximately 2.7 billion dollars, and are expected to remain at about this level until 2020. Public data from the Decision Resources web site forecast the sales to decline slightly to 2.6 billion dollars by 2026 as a result of patent expiry and generic erosion before rising again. The upcoming patent expirations of high-profile products such as Azilect, Stalevo and Comtan will impact the market revenue negatively. However, the market growth could be significant if there were new breakthrough drugs for the PD. Pramipexole (Mirapex, Boehringer Ingelheim) was the leading branded dopamine agonist, with sales of 490 million dollars in 2009 prior to patent expiry in 2010. Growth will be driven by the introduction of new therapeutic modalities that address the significant unmet medical needs, counterbalanced by the fact that many of the current products are or will become generic. The new entrants will be competing against generic products, so their profiles need to be clearly superior over the existing treatments in order to command a premium price.

In the US, the annual economic burden for PD has been estimated at 14.4 billion dollars in 2010, equating to approximately 22800 USD per patient (2). Overall, annual medical costs for PD patients are around 8.1 billion dollars higher than expected from a comparable PD-free population. It has been calculated that slowing disease progression by 20 % would realize a net monetary benefit (NMB) of 60 657 USD per patient (or 75 891 USD if lost income is included) (3). Halting disease progression at diagnosis would result in total savings of 442 429 USD per patient.

New therapeutic modalities that improve control of motor symptoms, delay the time to use L-Dopa, reduce troublesome side effects, treat some of the non-motor symptoms such as dementia, depression, sleep disorders, and which slow progression of the disease are needed and will drive market growth. Drugs which meet these unmet medical needs are expected to command a premium price and are expected to be reimbursed. Tozadenant (SYN115) is targeting several of these unmet medical needs in the treatment of Parkinson's. Tozadenant (SYN115) also has the potential to treat drug-induced dyskinesias in schizophrenia and other psychoses, which may affect 10-12 per cent of this patient group. The global antipsychotic market was worth USD 25.4 billion in 2010.

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Parkinson's disease is one of the most common neurodegenerative disorders occurring with an incidence second only to that of Alzheimer's disease.

Due to the nature and prevalence of PD, there's a huge market opportunity for any drug that can make a difference in patients' lives.

The amount of patients is growing rapidly due to the ageing population in Western countries.

Data suggest sales of PD drugs were $2.7 billion in 2010 and are forecasted to fall slightly to $2.6 billion by 2026 as a result of patent expiry and generic erosion before rising again. However, the market growth could be significant if there were new breakthrough drugs.

The economic burden for PD is huge, which means that the pricing potential of drugs that make a difference is very high. Drugs which meet the unmet medical needs are expected to command a premium price and are expected to be reimbursed.

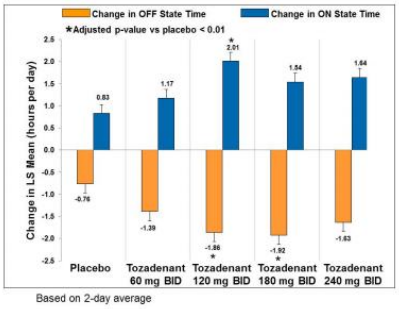
Tozadenant (SYN115) is targeting several of these unmet medical needs in the treatment of Parkinson's. Tozadenant (SYN115) also has the potential to treat drug-induced dyskinesias in schizophrenia and other psychoses.

Product profile for tozadenant (SYN115) – robust data from Phase 2 studies

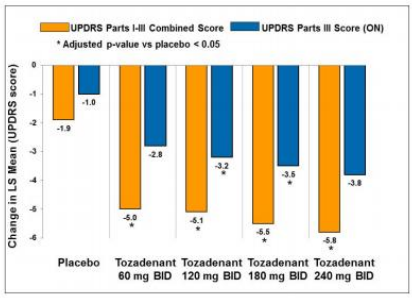
SYN115 is an orally administered, potent and selective inhibitor of the adenosine 2a (A2a) receptor that is being developed initially for the treatment of Parkinson's disease, but may also have utility in other CNS disorders. A2a receptors are expressed in high concentration in the striatum of the brain and there is an emerging body of evidence that they play an important role in regulating motor function. SYN115 blocks the effect of endogenous adenosine at the A2a receptors, resulting in the potentiation of the effect of dopamine at the D2 receptor and inhibition of the effect of glutamate at the mGluR5 receptor. This enables restoration of motor function in Parkinson's disease patients without the induction of troublesome dyskinesias.

SYN115 has the potential for use as mono-therapy or adjunctive therapy in combination with L-Dopa and dopamine agonists for the treatment of the motor and non-motor symptoms associated with Parkinson's disease. SYN115 may also have neuroprotective effects, which raises the possibility that it could slow the deterioration of dopamine producing cells and modify disease progression – a holy grail in Parkinson's disease. However, at this point this is only a possibility - there is no clinical evidence to support it.

SYN115 has been studied in a single ascending dose study, two multiple ascending dose phase 1 studies, and a phase 2a study in L-Dopa treated subjects with mild-to-moderate Parkinson's disease. SYN115 has been shown to be safe and well tolerated. The results of phase 2a showed that SYN115 enters the brain and causes changes in functional activity in specific regions associated with motor function and cognition. Improvements in various clinical assessments of motor function and cognition have also been demonstrated.



Mean Change from Baseline to End of Treatment (Week 12) in OFF and ON Time (mITT Population)



UPDRS Parts I–III and Part III—Change from Baseline to End of Treatment (Week 12) (mITT Population)

Exhibit 2. *The Phase 2 results of tozadenant have been robust.* *Source: company materials*

In another study, tozadenant displayed clinically relevant and statistically highly significant effects on PD across multiple pre-specified evaluation metrics including: a decrease vs. placebo in 'off' time, an increase in 'on' time, an improved score on UPDRS part III and UPDRS parts I-III combined, as well as improvements on clinician- and patient-assessed global impression scores. Additionally, the study identified the minimally efficacious and maximum feasible dose levels, as well as clinically useful target doses for Phase 3.

In general the clinical data of tozadenant has been very promising so far, which gives the drug high potential. The phase 2b study shows that tozadenant decreases "off-time" (of L-Dopa) by more than 1 hour when added to every other medicine that currently can be used to optimize PD therapy. This is a very worthwhile addition. However, the critical phase 3 hasn't been started yet, so there's still a lot of uncertainty regarding the eventual profile of tozadenant.

SYN115 is a potent and selective inhibitor of the adenosine 2a (A2a) receptor that is being developed initially for PD. Its mechanism of action should enable restoration of motor function in PD patients without the induction of troublesome dyskinesias.

SYN115 has the potential for use as adjunctive therapy in combination with L-Dopa and dopamine agonists for the treatment of the motor and non-motor symptoms associated with Parkinson's disease.

SYN115 may also have neuroprotective effects, which raises the possibility that it could slow the deterioration of dopamine producing cells and modify disease progression.

The results of Phase 2a showed that SYN115 enters the brain and causes changes in functional activity in specific regions associated with motor function and cognition. Tozadenant has also displayed clinically relevant and statistically highly significant effects on PD across multiple pre-specified evaluation metrics as well as improvements on clinician- and patient-assessed global impression scores.

Currently it seems that tozadenant can provide a significant addition to PD therapy, but the pivotal P3 studies are still ahead.

There are lots of therapies in the PD pipeline…

Parkinson's disease is normally treated using combination therapy and it is anticipated that Tozadenant (SYN115) may be used in conjunction with existing (typically L-Dopa) and complimentary novel mechanisms. The current PD pipeline reflects a shift in focus to long-term PD management, marked by the development of key pipeline candidates targeting levodopa-associated motor complications. These products will have the potential to change the future treatment algorithm as side effects of dopaminergic therapies become more manageable. The A2a antagonists represent a novel mechanism with the potential for treating both motor and nonmotor symptoms of the disease and for slowing disease progression. There are lots of competitors in the pipeline, which is natural for a market like PD.

There are lots of competitors in the pipeline, which is natural for a market like PD.

…but only one direct competitor

The most direct competitor for tozadenant is istradefylline (Kyowa Hakko Kirin), which is a "first-in-class" adenosine A2A receptor antagonist antiparkinsonian agent. It has the same mechanism of action as tozadenant. Investigators hope that this drug will suppress dyskinesia, the involuntary movements caused by PD medications, as well as ease the motor symptoms of Parkinson's itself. Kyowa Hakko Kirin has received approval for Istradefylline in the adjunctive treatment of PD in Japan. Istradefylline has been marketed as the brand name NOURIAST® in Japan since May 30, 2013. A New Drug Application was also filed in the US a long time ago, but the FDA issued a non-approvable letter in February 2008; the letter questioned whether the efficacy findings support the clinical utility of the drug. At least the first attempt for the US market was a failure. However, currently it is expected that the drug will be progressing to phase 3 studies in US and Europe in order to enter these markets later.

Perhaps the most direct competitor for tozadenant is Istradefylline, which is a "first-in-class" adenosine A2A receptor antagonist antiparkinsonian agent. It has the same mechanism of action than tozadenant. Istradefylline has been marketed as the brand name NOURIAST® in Japan since May 2013.

The drug was filed in the US long time ago, but the FDA didn't approve it in 2008. They questioned whether the efficacy findings support the clinical utility of the drug. Now the drug is expected to do the Phase 3 study again in the US and Europe in order to enter these markets later.

The results of Istradefylline, for example efficacy or possible toxicity, are not comparable to tozadenant. However, the studies performed on tozadenant so far have shown significant results, so we believe that the "efficacy problem" of Istradefylline isn't relevant for tozadenant. Also, if there were to be significant problems with the mechanism of actions, one could speculate that 1) Istradefylline wouldn't have been approved in Japan and 2) it wouldn't be progressing to Phase 3 in order to enter the US and EU markets. There's always the possibility that the company made mistakes in the phase 3 studies and therefore couldn't provide the necessary results for the FDA.

Drugs with related treatment goals

There are naturally many drugs with somewhat similar treatment goals. Azilect® (Teva) is an MAO-B inhibitor, a medication that blocks MAO-B and allows more dopamine to be available for use in the brain. Azilect is currently approved for the treatment of the signs and symptoms of Parkinson's disease both as initial monotherapy and as an add-on treatment to Levodopa later in the disease. Azilect helps preserve both a patient's own dopamine and dopamine derives from the medicine; it has a novel dual mechanism of action based on the enhancement of the dopaminergic function (through potent reversible inhibition of MAO-B and of dopamine uptake) and inhibition of the excessive release of glutamate. It is also designed to increase "on-time" and decrease "off-time" associated with Levodopa in the middle and late stages of PD. Like tozadenant, this drug should be used as an adjunct treatment, meaning it would be taken in addition to Levodopa and other existing PD medications.

MAO-B inhibitor Azilect is currently approved for the treatment of the signs and symptoms of Parkinson's disease both as initial monotherapy and as an add-on treatment to Levodopa later in the disease. It is also designed to increase "on-time" associated with levodopa in the middle and late stages of PD like SYN115.

Azilect, which is a part of Teva's central nervous system (CNS) portfolio, posted sales of 420 million dollars in 2012, up 7%. Rasagiline was originally approved to treat Parkinson's both in the early stages (used alone) and in the later stages (as an adjunct to Levodopa and other therapies), and is now being studied for its effects when given in combination with dopamine agonists. Azilect is currently in a Phase 4 study, which is being conducted to evaluate the effect of Azilect on cognitive function in adults with mild cognitive impairment (MCI) in Parkinson's disease (PD-MCI). The drug's next patent is set to expire in 2016, and after this a generic version could become available.

The symptomatic therapies being studied include several reformulations of Levodopa, which aim to address problems associated with current formulations, such as wearing-off. One example of such a medication is Rytary (Impax Laboratories). Rytary is an extended release capsule formulation of

While Azilect isn't a direct competitor, it is one of the drugs with similar treatment goals. It will be generic by the time tozadenant will possible be at the market, so it could affect the pricing potential. Tozadenant must have a significantly better profile in

carbidopa and Levodopa in development for the treatment of Parkinson's Disease. It has a mechanism that releases the compound slowly into the bloodstream throughout the day, rather than all at once, thus requiring a person to take fewer pills. Its goal is to provide continuous amounts of Levodopa to avoid wearing-off.

order to command a significant premium.

Naturally there are many other drugs further along in the pipeline, as this is a huge market with significant unmet needs. We cannot go through all of them here, but the following table consists of the most relevant drugs still in the development pipeline.

Naturally there are many other drugs further along in the pipeline, because this is a huge market with significant unmet needs.

Compound (Company)	Mechanims of action	Status
Istradefylline (Kyowa Hakko)	Adenosine A2A receptor antagonist	Approved in Japan, possible progressing to P3 in EU and US
Safinamide (Merck Serono / Newron)	MAO-B / dopamine uptake / glutamate release inhibitor	P3-ready, has submitted for EU MAA
Fipamezole (Santhera)	Alpha 2 adrenoceptor antagonist	P2, no progress reported in a long time
Dipraglurant (Addex)	mGluR5 modulator	2
Pardoprunox (Abbott)	Mixed partial agonist (D2, NA, 5HT-1a)	2
IPX066 (GSK/Impax)	Controlled Release carbidopa + levodopa	PR
VR-040 (Vectura)	Inhaled apomorphine (dopamine D2 agonist)	2
XP-21279 (XenoPort)	L-DOPA pro-drug	2
PD-02 (creatine monohydrate) (Avicena)	Antiapoptotic agents / neuroprotectants	3
AV-201 (Sanofi)	Gene therapy	2
ProSavin (Oxford BioMedica)	Gene therapy	2
NLX-P101 (Neurologix)	Gene therapy	2
Cere-120 (Ceregene)	Gene therapy	2

Table 3. *Drugs under development for Parkinson´s disease.* *Source: Company information*

Considering the big picture, there are naturally also drugs that are targeting a cure for PD, which is naturally the ultimate goal. If the cause of the neurodegeneration can be identified, perhaps a specific treatment can be developed to slow, stop or reverse its process. Future treatment strategies may include the delivery of substances or genetic material directly to the brain. In animal models of neurodegenerative diseases, several neurotrophic factors have proven highly efficacious. However, these techniques are in the earliest stages of development and the likelihood of success at this point is very low. One example of a more ambitious program is from a Finnish company Hermo Pharma that has proprietary neurotrophic factor CDNF is in late preclinical development with an aim to start first human studies in Parkinson's disease in 2014.

Considering the big picture, there are naturally also drugs that are targeting a cure for PD, which is naturally the ultimate goal. However, these treatments are in the earliest stages of development and the likelihood of success is very low.

Potential competitor preladenant was discontinued by Merck

Pharma company Merck declared in May 2013 that it was going to discontinue the clinical program for preladenant, Merck's investigational adenosine A2A receptor antagonist for the treatment of Parkinson's disease (PD). An initial review of data from three separate Phase 3 trials did not provide evidence of efficacy for preladenant compared with placebos. Based on these results, Merck decided to discontinue the extension phases of these studies and no longer plans to pursue regulatory filings for preladenant. This drug was considered to the perhaps the most significant competitor for tozadenant, so its failure could be considered to be positive for Biotie. This is especially due to the fact that the problem was with efficacy; the decision to discontinue these studies is not based on any safety finding. Since tozadenant's efficacy data has been solid so far, there's no reason to believe that the mechanism of action wouldn't be functional.

Perhaps the most significant competitor for tozadenant was preladenant. It was discontinued last year, after the Phase 3 trials did not provide evidence of efficacy.

The road ahead after UCB's decision

Before we can make any meaningful estimates on the possible net sales of tozadenant, royalties or milestone payments to Biotie, or give the drug a value, we must make some assumptions concerning the road ahead. After UCB's decision to return the rights to Biotie, the task got a lot more difficult.

Biotie had originally licensed to UCB Pharma worldwide exclusive rights to tozadenant in 2010. In February 2013 the parties amended their original license agreement to such that Biotie will also conduct Phase 3 development of tozadenant in return for additional payments from UCB. These were related to defined development, and regulatory and commercialization milestones. Under the terms of the original agreement UCB has made a one-time payment of 20 MUSD to Biotie, and Biotie remained eligible to a potential additional 340 MUSD in future milestone payments. Under the revised agreement, Biotie was eligible to additional payments in the low triple digit millions in total over the next six years, which practically meant that UCB would have paid for the R&D expenses of phase 3.

After UCB's decision to return the rights to Biotie, we are forced to also make assumptions also concerning the future partner of Biotie. Under the terminated partnership agreement UCB would have paid for the R&D expenses of Phase 3.

Biotie needs to find a suitable partner prior to P3 studies

Because Biotie doesn't have the resources to execute the phase 3 studies without outside funding, or at least it would have to make some large financial arrangements, it needs to find a partner first. We believe that tozadenant is an attractive asset for many companies, so there should be demand for it. However, it is extremely difficult to make assumption on the agreement terms of a possible contract. Tozadenant has developed further as an asset after the original deal with UCB and the phase 2 data was strong, so theoretically it should have a better bargaining power than before. However, a partner backing out of a development project is never a positive signal, no matter what the reasoning behind it is.

In the following table we have tried to demonstrate the difference between "big pharma" and a smaller pharmaceutical company as a potential partner. While all this is speculation at this point, we wanted to point out some key differences. The main one is that a big pharma company would have the resources, if it chose to do so, to conduct larger and more expensive phase 3 studies with a significantly wider scope (also earlier stage than in Phase 2). Just to give a reference point, these kinds of studies could cost around 300 MEUR, while a simple phase 3 study could be done with around 100 MEUR. With a wider scope tozadenant could get a wider usage and "labeling" for the drug, giving it a larger market potential. Naturally this would happen only if the data would support it. The presented payment structures are naturally only assumptions at this point; the main point to understand that no company is doing charity here. The higher the expenditure, the larger share of potential profits the company is expecting.

Biotie doesn't have the resources to execute the Phase 3 studies without a partner, which means that the first priority after the end-of-Phase 2 meeting has to be finding a new partner.

Tozadenant has developed further as an asset after the original deal with UCB and the phase 2 data was strong, so theoretically it should have better bargaining power than before.

However, a partner backing out of a development project is never a positive signal, no matter what the reasoning behind it is.

In table 4 we have tried to demonstrate some of the major differences between "big" and "small" pharma companies from the partnering perspective.

Options	1. "Big pharma"	2. "Small pharma"
Payment structure	Possible significant up-front, but low royalties	More focused on milestone payments and royalties
P3 structure	Large studies covering most of the foreseeable potential	Narrow scope with the same focus as in P2
Market potential	Huge proving a superior profile	Significant even with the limited target group
Potential for Biotie	Very significant despite the lower share of the profits	Significant - royalties could be very significant if successful

Table 4. *Simplified example of different partner profiles.* *Source: Inderes*

Assumptions and the financial estimates

It will be years before tozadenant will be in the markets, and the profile of the drug is still to be determined. Making the financial estimates for tozadenant is also very difficult because of the partnering situation. We have made our estimates with the assumption that Biotie will make a similar partner agreement as it had with UCB. This would be more in the "small pharma" category if we reflect on the earlier chapter.

We are forced to make some very large assumptions in order to evaluate the potential of tozadenant.

Naturally there are also many other assumptions that we have to make in order to evaluate the value of tozadenant. The most important assumptions have been opened up in the following table.

Main assumption behind our Tozadenant estimates (base case)	
Estimated number of patients	Roughly 7-10 million people have Parkinson's disease globally, at least 1 million in US
Drug treatment rate %	70 % - 80 %
Market size	2.7 billion dollars in 7 major countries. Estimated to grow to 5 billion in 10 years.
Patients receiving drugs	Possible around 5-8 million, growing rapidly due to the ageing of population
% using Tozadenant	Slowly increasing and reaching 15 % by 2026 - potentially higher
Patients using Tozadenant	We are using 560 000 for now, but this depends on the profile
Effective annual cost / patient	2580 USD / person / year (around 7 USD per pill and a day globally)
Peak annual sales	1400 MUSD, depends heavily on the profile: whether suitable also for early stage PD
Royalty rate %	10 % is our estimate, difficult to estimate at this point
Peak annual royalties	105 MEUR
Milestones (MEUR)	50 MEUR are expected to be realized, maximum probably much higher
Used WACC in discounting	16 %, which includes a significant risk premium
Terminal value	After the IPR protection ends, we are estimating very little cash flow

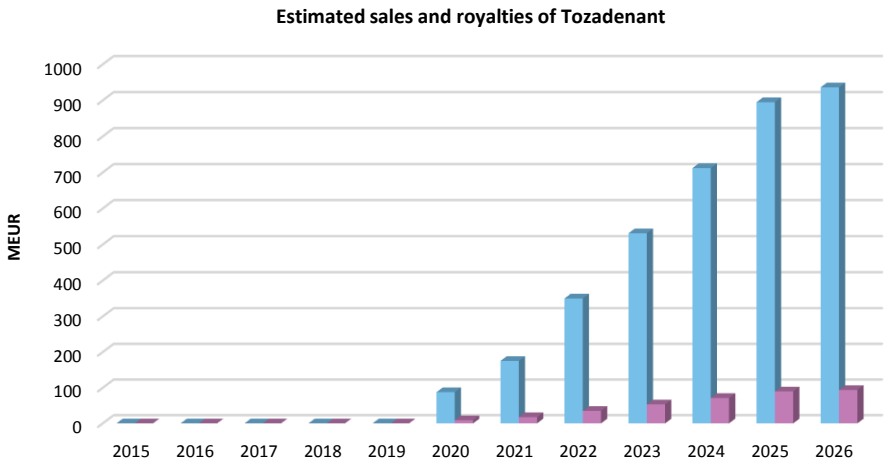
Exhibit 2. *Summary of assumptions to model Tozadenant forecasts* *Source: Inderes*

Some of the most important assumption that we have used behind the valuation model are explained in the Exhibit 2.

The figures clearly demonstrate the huge potential of tozadenant. Because of the very large market demand of Parkinson's, any drug that can bring significant benefits to large amount of patients can have annual sales above one billion dollars.

The figures clearly demonstrate the huge potential of tozadenant. Because of the very large market demand of Parkinson's, any drug that can bring significant benefits to large amount of patients can have annual sales above billion dollars.

We have modeled the net sales, which are naturally used to model the royalties, in the following way. Due to the very high uncertainty, these estimates should be considered only as scenarios that should demonstrate the sales potential. We are expecting the launch of tozadenant to be around 2019-2020 and we are modeling the sales to start in the year 2020.



Graph 7. *Estimated sales and royalties of tozadenant.* *Source: Inderes*

Because of the very large peak sales, the value of tozadenant is naturally very significant if the drug is successful. Therefore the current value is determined largely by the probability of success.

Due to the very promising clinical data, we are reasonable confident regarding the clinical success of tozadenant. We think the probability of clinical success is relatively high.

However, there's also always a significant commercial; in addition there's the risk regarding partnering. Due to these risks the overall probability of success is drawn down and might only be around 1/3 or 30-35 %. We are currently using a 30 % probability of success. This is a cautious estimate considering the current profile, but we like to be prudent at this point.

The value of tozadenant (for Biotie)

Because of the very large peak sales, the value of tozadenant is naturally very significant if the drug is successful. Therefore the current value, calculated by rNPV, is determined largely by the probability of success. Due to the very promising clinical data, we are reasonably confident regarding the clinical success of tozadenant. We think the probability of clinical success is around 2/3, which is relatively high. However, just getting a "mediocre" profile wouldn't necessary mean a successful launch. There's also always a significant commercial risk, and in addition to this there's the risk regarding partnering (meaning financing). Due to these risks the overall probability of success is drawn down and might only be around 1/3 or 30-35 %. We are currently using a 30 % probability of success. This is a cautious estimate considering the current profile, but we like to be prudent at this point.

Tozadenant is currently number two in the company's most valuable parts list. It has a huge potential, but the value is pushed down by the large uncertainty. Our opinion on the rNPV is around 47 MEUR, but the value would already increase if the partnering situation is rectified and the financing is resolved with good terms. The next significant value infliction points are the end-of-phase 2 meeting with the FDA and the partnering, which is hopefully solved soon after the meeting.

Value of tozadenant	
Status	Phase 3-ready
Probability of success (%)	Possible 30 % (partnering, clinical & commercial risks)
Estimated launch year	2020
Estimated peak market share	Possible significant in terms of value
Estimated royalty	10 %
Estimated peak sales	Easily higher than billion euros, if the profile is favorable
Patent expiry	2031
Estimated value (rNPV)	47 MEUR

2.3 SYN120 for the treatment of Alzheimer's disease

Alzheimer's disease is the leading cause of dementia in the ageing population and represents a huge social and economic burden. Currently there are few options for patients and the efficacy of products commonly used today is hindered by their unfavorable side effect profile. This basically means that the market opportunity regarding treatment of Alzheimer's is huge. SYN120 specifically targets a class of receptors in the brain that are involved in cognition. This specificity could help reduce the risk of peripheral side effects, potentially giving SYN120 a broader therapeutic window than current therapies through the reduction of debilitating symptoms of this disease.

Biotie had been seeking a development partner for SYN120 since June 2012 when Roche decided not to exercise its opt-in right for further development of the compound for strategic portfolio reasons. According to the company licensing discussions were at an "advanced stage". However, it seems that no suitable offer arrived, since the company has now decided that it will do further internal development of SYN120. We assume that the terms of the offer were simply not financially attractive to Biotie (there is an estimated 2% pay-away to Roche, the originator of the compound) at this stage.

This means that there will be an extra investment, which will be funded by current cash and Selincro revenues, to generate a phase 3-ready asset and secure a license on more lucrative terms for Biotie. This is naturally also a risk, if the development process wouldn't create the expected positive results. SYN120's dual activity offers significant differentiation from the competitors, so there's definitely potential here. Still, we'll wait for the results before assigning higher value for the drug.

Alzheimer's disease is the leading cause of dementia in the ageing population and represents a huge social and economic burden. The market opportunity regarding treatment of Alzheimer's is huge.

SYN120's dual activity offers significant differentiation from the competitors. After lengthy partnering negations, Biotie decided to invest in SYN120 and is attempting to make it a Phase 3-ready asset before partnering.

About Alzheimer's disease (AD)

Alzheimer's disease is characterized by a progressive, irreversible decline in memory and cognitive function. Symptoms typically start to appear after the age of 60, but it can arise in younger individuals. Ultimately the continued loss of function significantly interferes with a person's daily life and activities until they require constant nursing care.

AD is a disease of advancing years, with incidence rates of 1.45 % in ages 54-74, 4.7 % in ages 75-84 and over 9 % in ages >85 years (10). AD is the largest single contributor to dementia, accounting for 60-80 % of all cases (6). Dementia has a global prevalence of 5-7 %, with significant regional variation (e.g. rising to >8 % in Latin America and falling to 2.4 % in sub-Saharan Africa) (4). Overall, around 35.6 million people (~0.5 % of world total population) currently suffer from dementia, with number predicted to double every 20 years (3). Dementia represents the leading contributor to disability in the elderly. The total number of AD patients is estimated to reach >81 million globally by 2040 (5). In the US alone over 13 million people will have AD by 2050 (9), up from current estimates of 5.4 million (6) which already represents 1 in 8 of the population. AD is the 6th leading cause of death in the elderly in the US, impacting over 45% of those aged >85 years (6).

In 2010, worldwide costs of dementia were estimated at >600 billion dollars (representing 1 % of global GDP); 70 % of these costs occurring in the US and Western Europe, even though ~54 % of all dementia cases occur in countries with low-middle income. The majority of costs were associated with social and informal care rather than formal medical expenses (3). In 2012, US costs for AD exceeded 200 billion dollars (6), even without fully accounting for the significant mental and personal "costs" to care givers. Indeed, it has been suggested that caregiver QoL, which correlates directly to the neuropsychiatric severity of AD, should be included in future estimates of drug therapy economic benefit (7).

Overall, some 75 % of AD patients will show symptoms of dementia, including agitation, depression and psychosis (1). There is some variation in the degree of these symptoms reported in the literature, which may be explained by the impact of disease severity and duration on those measures. In late onset AD, over 50 % show symptoms of psychosis (8) while in mild-moderate AD only 20 % had these symptoms (2). Overall, psychosis occurs in 40 % of AD patients, including hallucinations in 23 % and delusions in 36.5 % (2). All studies agree that the occurrence of psychosis is linked to more rapid cognitive decline (1, 2, 8) and increased likelihood of institutionalization. Although delusions and hallucinations show different time courses and are not directly correlated, once present the symptoms persist and will reappear in 95 % of patients within 1 year of any remission (2). The symptoms are a major contributor to poor QoL for both the patient and the caregiver(s) (2).

Alzheimer's disease is characterized by a progressive, irreversible decline in memory and cognitive function. Symptoms typically start to appear after the age of 60. Overall, around 35.6 million people currently suffer from dementia, with the number predicted to double every 20 years. AD is the 6th leading cause of death in the elderly in the US, impacting over 45% of those aged >85 years.

Worldwide costs of dementia are huge and a cure for AD would be extremely valuable. In 2012, US costs for AD exceeded 200 billion dollars.

Overall, some 75 % of AD patients will show symptoms of dementia, including agitation, depression and psychosis.

Treatment of AD

There are no therapies that cure the disease currently. Existing therapies are targeted at symptomatic improvement of cognitive function and have significant limitations, but the sales figures are still impressive. The acetyl cholinesterase inhibitors that increase the concentrations of acetylcholine represent the main therapeutic class available today. Generic acetylcholinesterase inhibitors are at the cornerstone of treatment. In 2012, total sales in the G7 were 5.9 billion dollars, of which cholinesterase inhibitors accounted for $4.3 billion (73 %). Aricept (donepezil, Eisai/Pfizer) is the largest branded product, selling 1.5 billion dollars in 2012, with generic donepezil adding a further 1.0 billion dollars. In addition Namenda, which modulates the effect of glutamate, is also approved. In part as a result of new therapies, the market is expected to grow to 14.2 billion dollars by 2020.

The acetyl cholinesterase inhibitors are not very effective and suffer from significant side effects, which themselves limit the efficacy of the compounds. This is in partly because acetyl cholinesterase is distributed throughout the body and not just restricted to the brain – as a result these compounds have significant peripheral effects. SYN120 is anticipated to be competitive as a result of greater efficacy and fewer side effects than with existing therapies.

Cognitive deficits associated with schizophrenia (CIAS) are now considered to be a core feature of the disease, affecting 75-85 per cent of patients. Even when the positive or negative symptoms of schizophrenia are controlled, patients still have deficits in executive function, which is important for normal activities of daily living and social functioning. The global antipsychotic market was forecast to be worth 21.2 billion dollars in 2011. Biotie has proposed Phase 2 study, which may start recruiting patients by the end of 2014, and is likely to focus on neuropsychiatric and cognition improvement in Alzheimer's disease.

The AD pipeline is very active with over 100 programs in development. However, it has been said that the AD is a "graveyard of drug candidates", because the success of recent developments has been anything but satisfactory – basically everything that had any significance in treatment has turned out to be a failure. This is why AD is considered to be a very challenging market. The recent failures of the promised disease-modifying therapies have thrown new life into symptomatic therapies with increased efficacy and better tolerability than current drugs. At present SYN120 is the only pipeline molecule with the potential to address both the cognitive and psychotic symptoms of AD.

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There are no therapies that cure the disease. Existing therapies are targeted at symptomatic improvement of cognitive function and have significant limitations.

Generic acetylcholinesterase inhibitors are currently at the cornerstone of treatment. In 2012, total sales in the G7 were 5.9 billion dollars, of which cholinesterase inhibitors accounted for $4.3 billion (73 %). The treatment is not very effective and there are significant side effects.

Cognitive deficits associated with schizophrenia (CIAS) are now considered to be a core feature of the disease, affecting 75-85 per cent of patients. Biotie has proposed a Phase 2 study, which may start recruiting patients by the end of 2014, is likely to focus on neuropsychiatric and cognition improvement in Alzheimer's disease.

The AD pipeline is very active with over 100 programs in development. The recent significant failures (and there are a lot) promised disease-modifying therapies has thrown new life into symptomatic therapies with increased efficacy and better tolerability than current drugs. SYN120 is still the only pipeline molecule with the potential to address both the cognitive and psychotic symptoms of AD.

SYN120 Product profile - dual activity is the key

SYN120 is an orally administered, potent and selective antagonist of the 5-HT6 receptor that is in development for the treatment of Alzheimer's disease and other cognitive disorders, including schizophrenia. 5-HT6 receptors are located exclusively in the brain and blocking them results in increased concentrations of acetylcholine and glutamate, two known pro-cognitive neurotransmitters. SYN120 is a third generation 5-HT6 antagonist that has been designed to be devoid of some of the cardiovascular side effects that have impacted this class of drugs. Moreover, the selective expressions of 5-HT6 receptors in areas of the brain important in cognition are expected to improve the efficacy and safety profile of SYN120, versus currently available therapies.

SYN120 is a third generation 5-HT6 antagonist that has been designed to be devoid of some of the cardiovascular side effects that have impacted this class of drugs. Beyond blocking the 5-HT6 receptor, SYN120 will also

The established wide therapeutic margin of SYN120 enables doses that are well tolerated, and beyond blocking the 5-HT6 receptor, will also robustly antagonize 5-HT2a receptors in the CNS. The latter mechanism of action has recently demonstrated encouraging efficacy in psychosis associated with Parkinson's disease. Thus, by appropriate selection of dose ranges, SYN120 could have a unique therapeutic profile combining procognitive and antipsychotic activities.

antagonize 5-HT2a receptors in the CNS. The latter mechanism of action has recently demonstrated encouraging efficacy in psychosis associated with PD.

The status of SYN120 clinical trial

SYN120 has earlier been studied in two placebo-controlled trials in which volunteers received SYN120 at doses more than 10-fold the anticipated therapeutic dose for up to 14 days. SYN120 was well tolerated and there were no observations precluding further development.

In July 2011, Biotie commenced a PET study to determine the dose required to occupy the 5-HT6 receptor in the brain and to establish therapeutic dose. Top-line results for the PET study were announced in March 2012. The study was conducted at the Johns Hopkins University School of Medicine in the United States and enrolled nine healthy volunteers who were treated with different doses of SYN120. The results demonstrate that target levels of receptor occupancy expected for efficacy can be achieved with SYN120 doses that are an order of magnitude lower than those that have previously been shown to be safe and well tolerated for up to two weeks in healthy older volunteers.

SYN120 was initially identified as a 5-HT6 antagonist, but further work has revealed genuine dual activity for SYN120, which is also a potent antagonist of the 5-HT2a receptor. This is important, as preclinical animal model research has shown that low doses of the compound can improve cognition, while higher doses show evidence of anti-psychotic activity. Therefore SYN120 holds potential to improve neuropsychiatric symptoms and cognition in Alzheimer's disease, and possible other neurodegenerative disorders.

SYN120 is currently transitioning into Phase 2 development. Preparations for a Phase 2 study in Alzheimer's disease have started, with the study expected to begin recruitment by the end of 2014.

SYN120 was initially identified as a 5-HT6 antagonist, but further work has revealed genuine dual activity for SYN120, which is also a potent antagonist of the 5-HT2a receptor. Therefore SYN120 holds potential to improve neuropsychiatric symptoms and cognition in Alzheimer's disease, and possible other neurodegenerative disorders.

SYN120 is currently transitioning into Phase 2 development. Preparations for a Phase 2 study in Alzheimer's disease have started, with the study expected to begin recruitment by the end of 2014.

Competition - the pipeline is very active, but SYN120 should have an unique profile

Currently there are no therapies that cure Alzheimer's, and the existing therapies have limited efficacy and significant side effects. Because of the magnitude of the unmet medical need this is an active area for many companies, so there's definitely a lot of competition. Like we mentioned earlier, the AD pipeline is very active with over 100 programs in development. Some companies are targeting therapies for slowing the disease and many are focusing on symptomatic relief. Still, currently SYN120 is the only pipeline molecule with the potential to address both the cognitive and psychotic symptoms of AD, which is the key difference with the competition.

During the past years there have been some encouraging developments for both 5-HT6 and 5-HT2a antagonists that provide some validation of the approach. Lundbeck successfully completed a 278-patient proof-of-concept phase 2 study, with its 5-HT6 antagonist (Lu AE58054), in moderate Alzheimer's disease (add-on to donepezil). When added on to the current gold standard treatment, Aricept, LuAE58054 showed clinical improvement, thus validating the concept that incremental therapeutic benefit can be achieved with this class of compounds. Three Phase 3 studies in mild-to-moderate Alzheimer's disease patients are currently underway.

Meanwhile, Pfizer's 5-HT6 antagonist PF-05212377 is undergoing a 342-patient Phase 2 study in mild-to-moderate Alzheimer's. Acadia Pharmaceuticals' pimavanserin, a 5-HT2a antagonist, reported positive Phase 3 data in improving psychosis in Parkinson's disease patients, being a single study the FDA has accepted as being sufficient for NDA filing (planned for H214). Acadia also recently initiated a Phase 2 trial in Alzheimer's disease psychosis.

During the past years there have been some encouraging developments for both 5-HT6 and 5-HT2a antagonists that provide some validation of the approach. Lundbeck's LuAE58054 showed clinical improvement when added with Aricept, thus validating the concept that incremental therapeutic benefit can be achieved with this class of compounds.

On the other hand Acadia Pharmaceuticals' pimavanserin, a 5-HT2a antagonist, reported positive Phase 3 data in improving psychosis in Parkinson's disease patients.

Class	Company	Status	Targeted to	Efficacy / relevancy
5-HT6				
Lu AE58054	Lundbeck	Phase 3 studies are underway	Significant improvement in cognitive performance when added to donepezil (Arizept).	Lundbeck has validated the concept that therapeutic benefit can be achieved with this class.
PF-05212377	Pfizer	In Phase 2		
5-HT2a				
pimavanserin	Acadia Pharmaceuticals	Phase 2-ready	Psychosis in Parkinson's disease; also in Alzheimer's disease	Positive P3 data in improving psychosis in PD patients; good possibility also for similar condition in AD
5-HT6 + 5-HT2a				
SYN120	Biotie	Progressing to Phase 2 soon	SYN120 is the only molecule currently in the pipeline with the potential to address both the cognitive and psychotic symptoms of AD	Good scientific proof of concept considering the above.

Table 5. *Scientific proof of concept of SYN120 is strong based on similar development projects.* *Source: Inderes*

Based on the recent results of Lundbeck and Acadia, we are relatively confident on scientific proof of concept of the drug of SYN120. The major question is whether these two "sides" can be combined successfully and prove the advantage of this.

While these competitors are ahead of SYN120 in the development process, their success gives more confidence in the scientific proof of concept of the drug. Now both the 5-HT6 (Lundbeck) and 5-HT2a (Acadia) approaches, which SYN120 combines, have been found to be valid at least in relatively wide trials. Naturally the patient population of Acadia's pimavanserin was psychosis in PD, but at least this gives a strong indication for AD patients also. As such, the action mechanism of SYN120 remains very promising and further internal investment is justified to enhance the value of the project. The chances of securing a partner for SYN120 would be significantly enhanced with positive phase 2 data. Based on the recent results presented by Lundbeck and Acadia, we are relatively confident on the scientific proof of concept of the drug of SYN120. The major question is whether these two can be combined successfully and proving the advantage of this.

Value of SYN120 for Biotie

Because SYN120 is still early in the development pipeline, its value is very difficult to determine. Like mentioned, SYN120 is expected to progress to Phase 2 studies in H2'14. Biotie is financing P2 without a partner, so there's a significant financial risk also involved. We believe the costs of Phase 2 to be around 20-30 MEUR, which is a significant investment for Biotie.

Value of SYN120	
Status	Phase 2-ready
Probability of success (%)	Around 20 % (clinical, financial & commercial risks)
Estimated launch year	2020
Estimated peak market share	Small - lots of competitors
Estimated royalty	12 %
Estimated peak sales	Huge market potential
Patent expiry	2030
Estimated value (rNPV)	25 MEUR

Due to the profile of the drug, we are relatively confident regarding the scientific proof of concept of SYN120. Both mechanisms of action have already been researched (5-HT6 Lundbeck and 5-HT2a Acadia) in relatively wide trials and the data has been positive. But in addition to the clinical risk that is still significant for a Phase 2-ready asset, there are financial and commercial risks. We are currently giving SYN120 a 20 % overall probability of success, which isn't very encouraging. The financial risk that Biotie is carrying is a significant part in the relatively low figures. Biotie also has to find a suitable partner for the Phase 3 studies; the logic is the same as with tozadenant. The Phase 3 studies are simply too expensive for the company to finance independently. The current value is determined largely by the probability of success, and if more positive data becomes available, the value would be increasing with the probability of success.

The nature of AD is relatively similar than that of PD (tozadenant). The market potential is huge and any drug that can bring significant benefits to the large amount of patients can have annual sales above one billion dollars. The potential peak sales are very large, but we believe it's too soon to model the possible future sales.

With the value of 25 MEUR, SYN120 is number three in the company's most valuable parts list. It has a huge potential, but the value is pushed down by the very significant uncertainty. The next significant value infliction point is the Phase 2 result that we'll have to wait for a long time. Phase 2 studies typically take 1-2 years, and since this a large study, most likely the study will take two years.

2.4 SYN117 (nepicastat) for the treatment of cocaine dependency

SYN117 (nepicastat) is a potent and selective inhibitor of the enzyme dopamine β-hydroxylase (DBH) which has potential application in the treatment of cocaine dependency. NIDA (National Institute on Drug Abuse) and Biotie are currently investigating the safety and efficacy of Biotie's nepicastat in the treatment of cocaine dependence in a Phase 2b study, which is fully funded by NIDA.

Because of this arrangement, Biotie doesn't carry the financial risks of the study - without the "free" funding the company probably wouldn't be doing the study. We believe that the risk of failure is very high due to the targeted group of patients and the nature of cocaine dependence; relevant data proving the efficacy is difficult to produce. However, in the current situation there's only upside for the company.

SYN117 (nepicastat) has potential application in the treatment of cocaine dependency. NIDA and Biotie are currently investigating the safety and efficacy of Biotie's nepicastat in the treatment of cocaine dependence in a Phase 2b study, which is fully funded by NIDA. Biotie still retains all rights.

Because of this arrangement, Biotie doesn't carry the financial risks of the study. We believe that the risk of failure is very high due to the targeted group of patients and the nature of cocaine dependence.

Profile of SYN117

Like many other addictions, cocaine dependency is driven by a dysregulation in the dopamine reward system. Mechanistically, inhibition of dopamine beta hydroxylase (DBH) by SYN117 increases levels of dopamine (which reduces the craving for cocaine) and reduces the levels of norepinephrine (which decreases the pleasurable responses to cocaine and the potential for stress induced relapse following withdrawal).

Biotie has conducted a placebo controlled phase 2a study in non-treatment seeking cocaine addicts. This study showed that SYN117 was safe and well tolerated when administered with cocaine and that SYN117 reduces the pleasurable response to cocaine.

In December 2011, Biotie signed a partnership agreement with the National Institute on Drug Abuse (NIDA) at the US National Institutes of Health. NIDA and Biotie are investigating the safety and efficacy of Biotie's nepicastat in the treatment of cocaine dependence in a phase 2b study; NIDA is funding the conduct of a randomized, double-blind placebo-controlled trial, lasting 11 weeks, in 180 treatment-seeking cocaine-dependent subjects using nepicastat supplied by Biotie. The study started in May 2013 and is being conducted at approximately 12 US clinics specializing in the treatment of drug dependence. Results from the study are expected in H1'15. It's important to note that Biotie retains all rights to Nepicastat, and will be able to use data from studies conducted with NIDA to support future potential regulatory submissions.

We are highly skeptical on the probability of success of the SYN117. The efficacy will be difficult to prove due to the nature of both the target group and the nature of the disease. However, if the phase 2 data is positive, Biotie would probably take nepicastat through to approval and potential commercialization. The treatment of cocaine dependency is focused on the group of specialized in the area. Therefore the target group of Biotie would be limited to these, not the GPs in general. This means that the profile would be suitable for Biotie's evolved strategy.

Like many other addictions, cocaine dependency is driven by a dysregulation in the dopamine reward system. SYN117 increases levels of dopamine, which reduces the craving for cocaine.

We are highly skeptical about the probability of success of the SYN117. The efficacy will be difficult to prove due to the nature of both the target group and the nature of the disease. However, if the Phase 2 data is positive, Biotie would probably take nepicastat through to approval and potential commercialization.

Market opportunity is probably limited

According to NIDA, over 20 million people in the US have tried cocaine and around 2 million are cocaine dependent. Cocaine is one of the most common illegal drugs in the US. The US would definitely be the key market of nepicastat, were it to be successful. While cocaine dependency represents a significant unmet medical need and has a large economic and social burden to society, we believe that the commercial market is very challenging and limited.

There are currently no approved therapies for cocaine dependency. Still, there are several medications marketed for other diseases (e.g. Vigabatrin, Modafinil, Tiagabine, Disulfiram, and Topiramate) have shown promise and have been reported to reduce cocaine use in controlled clinical trials. Among these Disulfiram (used to treat alcoholism) has produced the most consistent reductions in cocaine abuse. New knowledge of how the brain is changed by cocaine is directing attention to novel targets for medications development and the compounds that are currently being tested take advantage of underlying cocaine-induced adaptations in the brain that disturb the balance between excitatory (glutamate) and inhibitory (gamma-aminobutyric acid)

According to NIDA, around 2 million people are cocaine dependent in the US. The US would definitely be the key market of nepicastat, were it to be successful.

There are currently no approved therapies for cocaine dependency, but there are several medications that have shown promise in treating cocaine dependency.

neurotransmission. Even though there are other possible treatments in the pipeline, we do not believe that the competitive situation would be a significant problem. None of the medications mentioned above have been very successful.

We believe that the potential target group would be much smaller than the 2 million mentioned above. Firstly, very few are diagnosed. The use of cocaine creates euphoria and high amounts of energy, which is why cocaine is mostly considered as a "party drug" which can greatly influence the perception of an addiction. Secondly, cocaine often isn't the biggest problem that the cocaine dependent people have. According to NIDA cocaine accounted for about 13 % of all admissions to drug abuse treatment programs in 2007 in the US. The problematic part is that the majority of individuals (72 %) who seek treatment for cocaine abuse smoke crack and are likely to be polydrug abusers, or users of more than one substance. Therefore a medicine that helps with the craving of cocaine isn't enough; it should help with the other drugs also (and possible alcohol). Considering that cocaine is the most expensive drug, those who are suffering by addiction might find a cheaper "replacement" in other illegal drugs.

As with any drug addiction, this is a complex disease that involves biological changes in the brain as well as social, familial, and other environmental problems. Therefore, treatment of cocaine addiction must be comprehensive and strategies need to assess the neurobiological, social, and medical aspects of the patient's drug abuse. Medicine is only a part of the process. Also, the nature of cocaine is different from that of e.g. alcohol. Because cocaine is illegal, its availability is naturally much lower. The temptation isn't waiting at the shell of every store, it requires a more specific setting.

Overall, we believe that the amount of patients potentially using nepicastat will be relatively low, if we assume that the profile of nepicastat is solely on the cocaine dependent (excludes the mixed polydrug uses). This takes away a lot of the market opportunity. On the other hand, the pricing of nepicastat could be very high. Due to the high cost of cocaine and therefore high cost of possible cocaine addiction, the possible pricing of nepicastat could be very high. Eventually this will be one part of the whole strategy, and we believe that it's premature to speculate it further at this point.

The market opportunity of nepicastat is probably limited. The majority of individuals (72 %) who seek treatment for cocaine abuse smoke crack and are likely to be polydrug abusers, or users of more than one substance. Therefore a medicine that helps with the craving of cocaine isn't enough; it should help with the other drugs also (and possible alcohol). Also, medicine is only a part solution for an addiction.

We believe that the amount of patients will be relatively low, if we assume that the profile of nepicastat is solely targeted at the cocaine dependent (excludes the mixed polydrug uses). This takes away a lot of the market opportunity. However, the pricing could be very high.

Value of nepicastat for Biotie

Due to the low probability of success, both clinically and commercially, we aren't giving nepicastat much value. Still, since NIDA is funding the Phase 2 studies and there's a possibility that Biotie could be holding the full rights of a Phase 3-ready asset in the coming years, it cannot be ignored completely. The key here is the "free" financing by NIDA, otherwise the project might even have a negative rNPV.

In our opinion the market opportunity is limited, unless nepicastat is proven out to be helpful also for other addictions. If nepicastat would be helpful only in the case of cocaine dependence, but couldn't help with other addictions that patients are relatively likely to have, it would be able to solve only one part of a larger problem. Naturally this could be helpful for a small group of people, but many who are suffering by addiction might find a cheaper "replacement" in other illegal drugs.

We are giving nepicastat a value of 5 MEUR for now. If the Phase 2 study would be successful (against the odds), the value could be significantly more.

Value of Nepicastat	
Status	Phase 2 ongoing
Probability of success (%)	5 %, very high risk due to the difficult target group
Estimated launch year	2020
Estimated peak market share	So far no competitors
Estimated royalty	Possibility of independent launch
Estimated peak sales	Small market, difficult to estimate
Patent expiry	Unknown at this point
Estimated value (rNPV)	5 MEUR

2.5 VAP-1 Antibody for inflammatory / fibrotic disease

BTT-1023 is a fully human monoclonal antibody targeting VAP-1 (vascular adhesion protein-1). VAP-1 is a completely new therapeutic target. The safety and efficacy of BTT-1023 has been investigated in small clinical trials in rheumatoid arthritis and psoriasis patients. Biotie is currently transitioning BTT-1023 into Phase 2 development in primary sclerosing cholangitis (PSC), a rare fibrotic condition of the liver. However, the financing of Phase 2 studies is still unclear. Biotie has stated that there are "advanced discussions" for non-dilutive co-funding for the study.

BTT-1023 is a fully human monoclonal antibody targeting VAP-1 (vascular adhesion protein-1). VAP-1 is a completely new therapeutic target.

When thinking about the potential of BTT-1023, it's worth noting that it could be classified as an "orphan drug". An orphan drug is a pharmaceutical agent that has been developed specifically to treat a rare medical condition, in this case PSC (an orphan disease, prevalence is probably around 1/10000). In the US and EU it is easier to gain marketing approval for an orphan drug, and there may be other financial incentives, such as extended exclusivity periods, all intended to encourage the development of drugs which might otherwise lack a sufficient profit motive. This together with the fact that PSC could be considered a life-threatening disease without a cure means that the pricing of the product could be very high. However, at this point the probability of success is very low.

Biotie is currently transitioning BTT-1023 into Phase 2 development in PSC, a rare fibrotic condition of the liver. However, the financing of Phase 2 studies is still unclear. Biotie has stated that there are "advanced discussions" for non-dilutive co-funding for the study.

BTT-1023 has been around for a long time; when Biotie was listed on the Helsinki Stock Exchange back in 2000, it was one of the company's drug development projects. We believe it's prudent to be very cautious when it comes to the value of BTT-1023. In our analysis we haven't included BTT-1023 in our NPV calculations - it's simply too early in the development process to make any realistic assumptions about the financial possibilities, so we have concluded that the value cannot be determined at this point. We would encourage investors to consider it as a free option. If it turns out to be successful in treating PCS, excellent, if it is discontinued, it doesn't influence our view of company's value. This naturally is based on the assumption that company doesn't make significant investments in the development of BTT-1023.

We haven't included BTT-1023 in our NPV calculations and we would encourage investors to consider it as a free option.

Vascular adhesion protein-1 (VAP-1) as a therapeutic target

A key factor in establishing and maintaining chronic inflammation is the excessive accumulation of white blood cells, or leukocytes, in the tissue. Leukocytes exit the blood stream and move towards the site of inflammation through a series of processes, including attachment to specific adhesion proteins. These proteins are often expressed in response to initial inflammatory signals. VAP-1 is an adhesion molecule expressed on the endothelial lining of blood vessels. An exciting feature of VAP-1 is that its expression is thought to be up regulated only at the site of inflammation, limiting potential side effects of a product targeting this pathway.

VAP-1 is an adhesion molecule expressed on the endothelial lining of blood vessels.

BTT-1023 product profile

BTT-1023 is a fully human monoclonal antibody that specifically binds to VAP-1. Biotie has previously demonstrated encouraging efficacy and safety for BTT-1023 in early clinical studies in rheumatoid arthritis and psoriasis patients and in a range of preclinical models of inflammatory diseases, including COPD and certain neurological conditions. More recently, Biotie has generated new data indicating that VAP-1, in addition to its clinically demonstrated role in inflammatory diseases, has an important role in fibrotic diseases. These data, generated in part in collaboration with National Institute for Health Research Liver Biomedical Research Unit at the University of Birmingham, UK, reveal significant potential for BTT-1023 in certain niche liver inflammatory fibrotic diseases.

BTT-1023 is a fully human monoclonal antibody that specifically binds to VAP-1. There could be potential BTT-1023 in certain niche liver inflammatory fibrotic diseases.

Biotie has completed three clinical studies with its VAP-1 antibody including a single dose, placebo-controlled study in healthy volunteers and two Phase 1b trials in patients with rheumatoid arthritis and psoriasis, respectively. These trials have shown that BTT-1023 is safe and generally well tolerated when administered intravenously (IV) at repeated doses of up to 8mg/kg.

Trials have shown that BTT-1023 is safe and generally well tolerated when administered intravenously with correct doses. However, there isn't proof of the efficacy of BTT-1023.

Although the Phase 1b trials were not designed to enable formal statistical evaluation of efficacy, in several assessments of treatment effect in the RA trial, including Disease Activity Score based on 28 joint assessment (DAS28) criteria and American College of Rheumatology criteria (ACR), the responses observed in patients taking higher doses of BTT1023 were greater than in the placebo

group, including several patients reaching an ACR50 response (a 50% reduction in their ACR score) during treatment.

In Q3'10 data from the Phase 1b trial in patients with psoriasis was reported. While the efficacy signals were not as robust as in the RA trial, there were several patients on the active drug that experienced an improvement in their condition. Two patients reported a transient exacerbation in their psoriasis symptoms after treatment had been completed; apart from these two cases, no serious or severe adverse events were reported.

Program status

Biotie is preparing for a Phase 2 proof of concept study with BTT-1023 in primary sclerosing cholangitis, a rare fibrotic disease of the liver affecting young adults. Discussions for non-dilutive co-funding for the study are at an advanced stage. Recruitment in the study is expected to start by the end of 2014. If the Phase 2 data would be successful, Biotie would most likely seek a partner for subsequent development.

Biotie is preparing for a Phase 2 proof of concept study with BTT-1023 in primary sclerosing cholangitis.

Market Opportunity - patient Population and Market Size

Liver diseases such as Nonalcoholic fatty liver disease (NAFLD) and nonalcoholic steatohepatitis (NASH) are the fastest-growing liver diseases in the United States and the western world, with an estimated 17 million cases of NASH in the United States in 2009; patients are at high risk for further liver damage, including fibrosis, cirrhosis, and even hepatocellular carcinoma (HCC). No FDA-approved treatment for NAFLD or NASH currently exists.

PSC and PBC are much less common, both meeting the criteria for orphan disease designation, but patient numbers are nevertheless significant. The unmet medical need is very great – PBC is the primary reason for liver transplants in the United Kingdom, and there is no FDA-approved treatment for PSC which has a median survival after diagnosis (without liver transplant) of 10-12 years. Significant opportunity exists for the treatment of fibrotic diseases of the lung, kidney and skin.

The prevalence of PSC is estimated to be around 1/10000 in general population. This means that it meets the criteria for orphan disease designation, but patient numbers are nevertheless significant and the unmet medical need is great.

There's no competition so far

Despite the high prevalence of fibrosis and its enormous impact on human health, there are currently no FDA approved agents that can prevent, arrest or reverse fibrosis. Biotie is not aware of any compounds in late stage clinical development for PBC or PSC, or of any other companies developing antibodies targeting VAP-1 for any indication.

While the VAP-1 treatment/molecule is certainly a long shot in the development pipeline, there's an interesting opportunity partly because Biotie might receive an orphan drug status for VAP-1. This is due to the small target group and would mean a very strong protection for the VAP-1. Basically it could be the only drug for the specific purpose for seven years in addition to the typical protection.

There are currently no FDA approved agents that can prevent, arrest or reverse fibrosis. Biotie is not aware of any compounds in late stage clinical development for PBC or PSC, or of any other companies developing antibodies targeting VAP-1 for any indication.

Too early for financial estimates and valuation

We haven't included VAP-1 in our valuation model at this point. We believe that VAP-1 is currently too early in the development pipeline in order to make any realistic financial estimates. With such a high uncertainty, the value would also be insignificant for Biotie. We will take another look when more information is released, but for now we are not giving VAP-1 development project any value.

We haven't included VAP-1 in our valuation model at this point; the uncertainty is so high that the value would be insignificant for Biotie anyway.

3. Biotechnology is a huge and booming business

Biotechnology is currently one of the hottest businesses there are, even though in Finland the picture is quite different. There is a large transformation in the pharmaceuticals business area, which is reflected on biotech companies. Big pharmaceutical companies have been very successful in the past. They have managed to develop very important drugs, so called blockbusters, and they have been enjoying a stream of patent protected sales until present days. Now the situation is changing and more and more critical patents are ending. "The big pharma patent cliff" is coming during the next few years.

Naturally this has already been noticed in the industry a long time ago. First the big pharma companies were investing heavily in order to find new blockbuster drugs, and repeat the success story of the past. During the last few years, or possible even a decade for some companies, they have found this strategy to be unsuccessful. There are no longer "low hanging fruits" that the early movers like Amgen in biotech enjoyed, and often the huge R&D investments have produced little or nothing. While there are still those who refuse to accept that the game has changed, many companies have cut their R&D "CAPEX" significantly during the last years and are currently focusing more in the cash flow. The drug development business that used to go forward with giant leaps (completely new discoveries and blockbuster drugs) is now taking more small, incremental steps. The giants of the industry are currently not built for this. Still the biggest value proposal is in own development, but the risk profile there looks to be changing to unfavorable.

This transformation of pharmaceuticals has created significant room on the markets and a new breed of more focused and specialized biotech companies have evolved. A specialty Pharma sector has been forming slowly over the years, but now the structure is changing quickly. Newcomers are taking smaller niches, specializing only in them and then selling the asset or collaborating in different areas. The different focus areas can be anything from early discover, different development phases or sales. Some companies will focus on tail-products, where the patents are ending. Different kinds of services businesses are now also everywhere. Even big pharmas are looking into small niches now - they seem to be going everywhere now, from academia to marketing, to find the next golden goose. Still the strongest area for big pharma companies is the latter part of the development process. These companies have the money and resources to do large Phase 3s and they also have the critical experience with regulators, which is one of the key parts in the whole process. Therefore it's typical that as the development progresses, the products are concentrated in fewer and larger companies, either through partnering or acquisitions.

Another key factor for the large cluster of small biotech companies has been venture capital (VC) funding, which has opened a lot of doors for smaller companies. VC funding and the feeding of the big pharma made this business boom, and it's currently one of the hottest segments in the world (excl. social media). The main clusters for the biotech boom are the Silicon Valley (as in the "normal technology") and Boston. There are also a growing number of companies in the San Diego area.

Perhaps to most successful biotech company is Amgen. A biotechnology pioneer since 1980, Amgen has grown to be the world's largest independent biotechnology company, has reached millions of patients around the world and is developing a pipeline of medicines with breakaway potential. The company discovers, develops, manufactures and markets medicines for grievous illnesses. It focuses solely on human therapeutics and concentrates on innovating novel medicines based on advances in cellular and molecular biology. Amgen's 2013 revenue was 18.7 billion dollars and its R&D expenses were approximately 3.9 billion dollars. The company's MCAP is around 94 billion dollars and it's listed on the Nasdaq with the ticker AMGN.

Other major companies in the biotech industry are companies like Gilead Sciences (primary areas of focus include HIV/AIDS, liver disease and serious cardiovascular and respiratory conditions), Merck KGaA (large portfolio), Biogen Idec (focuses to diseases such as multiple sclerosis, non-Hodgkin's lymphoma, rheumatoid arthritis, Crohn's disease, and psoriasis), Celgene (cancer and immune-inflammatory related diseases), UCB (ex-partner of Biotie), Ipsen (oncology, endocrinology, and neuromuscular disorders), Vertex Pharmaceuticals (viral diseases, multidrug resistance in cancer, inflammatory and autoimmune diseases, and neurodegenerative diseases), Regeneron Pharmaceuticals (cancer, eye diseases, and inflammatory diseases) and Alexion Pharmaceuticals that

The biotechnology business is going through a transformation - "The big pharma patent cliff" has been changing the whole business area and biotech has been a very active business area in last few years.

The drug development business that used go forward with giant leaps (completely new discoveries and blockbuster drugs) is now taking more small, incremental steps. The giants of the industry are currently not built for this.

This transformation of pharmaceuticals has created significant room on the market and a new breed of more focused and specialized biotech companies have evolved. The specialty Pharma sector has been forming slowly over the years, but now the structure is changing quickly.

VC funding and the feeding of the big pharma made room for this business boom, and it's currently one of the hottest segments in the world.

Perhaps the most successful biotech company is a business pioneer Amgen. However, there are lots of other large companies as well. The biggest one measured by market cap is Gilead Sciences.

develops C5 complement inhibitors and Apogens which are two classes of potential therapeutic compounds designed to selectively target specific disease-causing segments of the immune system. There are just to name few of the bigger players in the field. We already mentioned companies like Hermo Pharma and Prexton Therapeutics as competitors in the Parkinson's side.

Company FY'13	Market Cap BUSD	Revenue BUSD	EBIT MUSD	Number of employees
Amgen	86	18.7	6165	20000
Gilead Sciences	115	11.2	4524	6100
Merck KGaA	39	15.3	3252	38154
Biogen Idec	66	6.9	2490	6850
Celgene	69	6.5	1980	5100
UCB	13	4.7	606	8224
Ipsen	3.9	1.8	280	4602
Vertex Pharmaceuticals	17	1.2	30	1800
Regeneron Pharmaceuticals	27	2.1	760	2340
Alexion Pharmaceuticals	26	1.6	576	1774

***Table 6**. Basic facts about some major biotech companies. Source: Thomson Reuters*

We are not going to through all the big pharma companies in this report, but just to get a basic picture we are going to mention some of the key players. These include Pfizer, Novartis, Roche, Merck & Co, GlaxoSmithKline and Sanofi. These are just a few of the players, and there are many more e.g. in Japan. Here we have mentioned only Otsuka Pharmaceutical that has the rights to Selincro in Japan and is therefore indirectly relevant to Biotie also.

Company FY'13	Market Cap BUSD	Revenue BUSD	EBIT MUSD	Number of employees
Pfizer	196	51.6	17213	77700
Novartis	193	58.8	11530	135696
Roche	192	52.4	19476	81769
Merck & Co	147	44.0	15615	76000
Glaxosmithkline	130	43.9	12756	99817
Sanofi	140	45.8	9337	112128
Lundbeck	5.0	2.8	386	5518
Orion	3.9	1.4	366	3519
Otsuka Pharmaceutical	19.3	12.9	1827	25330

***Table 7**. Key figures of"Big pharmas" and selected companies. Source: Thomson Reuters*

Lundbeck's MCAP is only roughly 3.6 BEUR, so it is actually very small compared to these giants in the industry. Just to give some kind of perspective, Lundbeck's MCAP is around 2.5 % of that of Pfizer, Novartis or Roche. Orion, definitely a well-known pharma company to Finnish investors, has a market cap of 3.9 BUSD. Orion is therefore at least in the same ballpark in size as Lundbeck.

We are not going to through all the big pharma companies in this report, but just to get a basic picture we are going to mention some of the key players. These include giants like Pfizer, Novartis and Roche – all have MCAPs of close to 200 BUSD.

Just to give some kind of perspective, Biotie's partner Lundbeck has a MCAP 5 BUSD – only 2.5 % of the MCAP of the giants. Finnish Orion is somewhat smaller than Lundbeck.

Merck, GlaxoSmithKline and Sanofi are also really big companies in the field.

3.1 Basic facts about the medicine development

There are certain facts about the business area of Biotie that investors should understand. Here's a short summary of them.

1. **Developing medicine is very expensive**

The average cost of one successful medicine has been estimated to be around a billion dollars. This is roughly the price of developing a new airplane and there are no guarantees of success even with this kind of investment. However, this "average" includes all the failures, so it doesn't actually requite a billion dollars to develop medicine. This is an estimated sum of all the R&D expenses in the sector divided by successful launches. If you think about the investment required by a single drug without any failures (home run with the first hit), the sum is probably a few hundred million per drug. For example, we believe that Biotie used less than 100 MEUR in the development of Selincro, roughly 25 MEUR in R&D costs, and 60 MEUR for different licensing costs. However, these are only our estimates and it's still very expensive to develop new medicine.

The average cost of one successful medicine has been estimated to be around a billion dollars due to many expensive failures.

2. **This is a very "risky business"**

Developing medicine is not only very expensive, it's also very uncertainty. Even if all the clinical studies would show great results, there are also "unknown" risks. For example, upon a new product launch one could find adverse side-effects of the medicine. If this were to be severe, the value of the whole product could be zero, even though you would have just invested hundreds of millions in the development process. This is why this business is very much about managing risks.

The risks of medicine development are very high and this business is very much about managing risks.

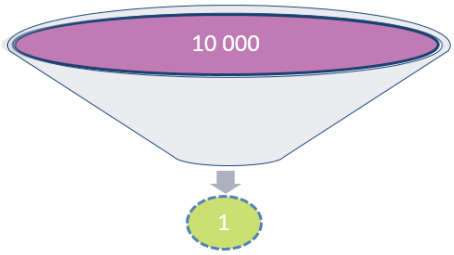
3. **The odds are against you**

Out of 10 000 discovered compounds, statistically only roughly three are ever brought to the markets as products. Out of these three, one might be roughly break-even and one unprofitable, when also considering the development costs. So on average only 1 out of 10 000 compounds eventually becomes a profitable products for the developers. Naturally these often become "blockbusters" that fund all the other unsuccessful projects, but it's still very risky game especially since smaller companies have limited pipeline.

Out of 10 000 discovered compounds, statistically only roughly three are ever launched to the markets as products, and only one is clearly profitable.

When thinking about the really rough probabilities of success, meaning from a specific development stage until a successful launch of a product, the averages are something like this:

Pre-clinical studies	5 %
Phase 1 ready	15 %
Phase 2 ready	40 %
Phase 3 ready	80 %
Marketing license	95 %



4. **It's all about the rights (IPR)**

In order to make significant profits with the ones who survive the cut, there has to be protection of the products. In general very few compounds are difficult to copy, so patents are critical in this business. It's worth noting that the lifetime of a patent is generally only 20 years, and since the development process is on average 15 years, there isn't much time to enjoy the "monopoly". However, there are different levels of protection. In the EU there's a 10 year protection for all the novel drugs. There's a similar system in Japan and somewhat weaker system in the US.

IPRs are a crucial in the biotech industry. There are different levels of protection. For example the lifetime of a patent is generally only 20 years, when the development process is on average 15

Drug patents are applied for at the Patent and Trademark Office who will make a decision as to if the patent should be granted. There can be differences among different countries. If it is approved, the patent is granted to the company and will last as long as 20 years from the filing date. It's important to notice that the time starts to count once to compound is first introduced, which is typically in the discovery phase. Since the average development process lasts 10-15 years, company will have only around 5-10 years of time to enjoy the protected sales. However, there might be some ways to get longer coverage. Exclusivity to the drug will vary and can last as long as 7 years depending on the type of drug it is.

It's also worth noting that during this time patients are accustomed to the specific product and its brand. Especially if the condition is life threatening, they are not going to change easily to the cheaper generic copy. Biological treatments are always the most difficult to copy and therefore they enjoy more "protection" also due to this. Still, once the patents run out and the generic competitors arrive to the markets, the profit margins shrink significantly.

years. This means that other protection is needed.

In the EU there's a 10 year protection for all the novel drugs. There's a similar system in Japan and a somewhat weaker system in the US.

Once the patents run out and the generic competition starts, the profit margins shrink significantly.

5. If you're going to fail, do it early

The costs of the development process accumulate over time, but they rise almost exponentially towards the end. In the pre-clinical stages the costs are typically measured in millions or tens of millions. When the clinical phases start, the medicine is tested on human trials that already increase the costs. The trials become larger and larger when moving on with the three phases and typically phase 3 involves thousands of participants. It's not really possible to create a reliable "average" since all the products are different, but as a rule of thumb: in Phase 1 we are talking about a figure in the low end of tens of millions, in Phase 2 the higher end of tens of millions and in Phase 3 the amounts rise up to hundreds of millions. The key point is this: if you're going to fail, do it early. The later it happens, the more money will be lost in the process. This also means that if the company doesn't believe in the medicine strongly, it won't go forward with it. No one is going into e.g. Phase 3 expecting negative results, so all the rejections (and there are many) in the latter phases are negative for the company.

The costs of the development process accumulate over time, but they rise almost exponentially towards the end. The pivotal Phase 3 studies typically produce roughly 2/3 of the overall costs of the process.

6. Gross margins are extremely high

Once the medicine has been developed, it's generally relatively easy and very cheap to manufactory. Therefore the cost of goods is very low, and the gross margins are extremely high. While you are enjoying the protection of patents, the more you sell, the more you make profits.

The gross margins of medicines are extremely high during the time they enjoy the protection of patents.

7. Pricing strategy is one of the key factors

Pricing is naturally one of the key components in financial success. Pricing includes a strategy and plenty of regulation in different markets. Typically there's a certain routine in the market launches; first the medicine is brought to the markets with higher prices because the pricing of others might be dependent on these references. Pricing is a part of the commercial stage and therefore it's often in the hands of the partners - and therefor is basically also a part of the partnering process. However, if the evolution of Biotie's strategy also takes the company to the commercial stage and marketing, the pricing strategy becomes more important. The prices of treatments can be very different in different continents: in the US the same treatment can cost 2-3 times the amount that it costs in Europe. This makes the US clearly the most important market for pharmaceuticals. In Japan the prices are generally between those of the US and Europe, where the prices are typically the lowest.

Pricing is one of the key components in financial success. The price can wary greatly between different markets; the same treatment often costs 2-3 times more in the US than in Europe. Japan is typically somewhere between these markets in regards to pricing.

8. Managing the risks and making the right investments

The management of biotech business is all about the risk management as well as making the right investments in the right development projects. Since the risk of failure is always significant in the development process, all the investments need to be considered by the risk/return profile. We would use the analogy of start-up investing in this business and could say that the management of

We would use the analogy of start-up investing in this business. The management faces a lot of similar decisions as a portfolio

Biotie faces a lot of similar decisions as a portfolio manager in the start-up sector. You need to make the right investments, but also be able to cut your losses early if the profile changes.

manager in the start-up sector.

9. Focus on progress, not the short-term earnings

While all the investors want to see earnings and dividends, quarterly results and even annual results in this business are almost meaningless. If the majority of company's products haven't been launched, the R&D costs will overshadow the revenues most of the time. However, the value of the products increases with every milestone that brings them closer to the launch. Favorable research results bring value to the products even though it doesn't bring sales.

Note also that many companies never bring in significant sales deriving from products. They develop the medicine to a certain point and sell it to the next company. If they have been successful, they will make money. There's an investment aspect in the business, which shouldn't be forgotten.

Quarterly results in this business are almost meaningless. Favorable research results bring value to the products even though it wouldn't bring sales in the near future.

10. Wide variety of companies in a hot sector

The biotechnology sector has a very large spectrum of different companies. There are huge pharmaceutical giants at the other end and a lot of small companies with a single project at the other (so called "one trick ponys"). Currently the activity in the sector is also huge. There has been a huge amount of public offerings especially in the US latterly. At the end of 2013 the biotech companies have been raising 50-100 million dollars every single day with both IPOs and secondary offerings in the US and, there are new companies listed all the time. The activity level is simple extraordinary right now, which of course makes the situation of Biotie also very interesting.

There are around 300 listed biotechnology companies on Nasdaq and around 100-150 listed in Europe. In addition there are perhaps 2000-3000 venture capital backed companies in the US and roughly 2000 in Europe. Still the largest ten companies have probably around half of the whole valuation of the sector. We argue that there are less than a hundred significant and noteworthy companies in this sector globally.

The largest single pharmaceutical market is the United States, which has an annual value of roughly 350 billion dollars. The European market is roughly 220 billion dollars in value and Japan around 110 billion dollars. Globally the market is close to 1000 billion dollars; according to the IMS 2012 figures the market was worth 962 billion dollars.

The biotechnology sector has a very large spectrum of different companies. There are around 300 listed biotechnology companies on Nasdaq and around 100-150 listed on Europe. Still we argue that there are less than a hundred significant and noteworthy companies globally.

The global value of the pharmaceutical market is close to 1000 billion dollars.

11. M&A activity is one of the key factors also for Biotie

There are lots of opportunities in both acquisitions and potential buyout candidates for Biotie. Naturally also different kinds of mergers are possible. While there's no pressure to act, generally a market value below 500 MUSD doesn't create interest in the US, which would support a growth strategy. There aren't many synergies on a project level or general level to be gained through acquisitions, but the diversification of risks and possible R&D would be gained through larger size.

M&A provides lots of possibilities for Biotie. It could be a buyer or a target for a larger company.

12. Biotech industry is interactive and has high visibility

The Biotech industry is very interactive and there's good visibility on the general activity of companies. Even though the level of disclosure varies widely between different companies, in general companies know relatively well what other companies have in the development pipeline. Clinical trials in patients (i.e. phase 2 and beyond) usually need to be registered in public databases, but especially big pharma may not disclose the mechanism of action of a candidate until Phase 3. They do not have a similar need to raise awareness or money, whereas smaller companies typically need to be more transparent. Scientific findings are naturally also presented and debated. Therefore all the companies should know reasonable well what others are up to, and there should be relatively few surprises in general.

The biotech industry is very interactive and there's good visibility into the general activity of the companies. The companies know relatively well what the others have in the development pipeline.

3.2 Biotie's partners

The most important partner for Biotie is currently Lundbeck who owns the global rights of Selincro. Before UCB's decision to return the rights to tozadenant to Biotie, it was another key partner for Biotie. Whoever will replace UCB regarding tozadenant, will be very important to Biotie. It's also worth noting that both Lundbeck and UCB are significant owner of Biotie. In addition there's NIDA for nepicastat, which is also interesting though mostly due to the possibility to carry significant R&D expenses without losing the rights. In the past Biotie has worked with companies like Roche.

The most important partner for Biotie is currently Lundbeck who owns the global rights of Selincro. UCB was another key partner prior to its decision to return the rights to tozadenant to Biotie.

Lundbeck – Selincro

Lundbeck is a global pharmaceutical company committed to improving the quality of life for people suffering from brain diseases. Lundbeck is engaged in the research, development, production, marketing and sale of pharmaceuticals across the world. The company's products are targeted at diseases such as depression and anxiety, psychotic disorders, epilepsy and Huntington's, Alzheimer's and Parkinson's diseases.

Lundbeck is a Danish pharmaceutical company that operates globally. The company's products are targeted at diseases such as depression and anxiety, psychotic disorders, epilepsy and Huntington's, Alzheimer's and Parkinson's diseases.

Lundbeck markets a number of different pharmaceuticals for the treatment of brain diseases. The most recently launched compounds include: Brintellix® (depression), Cipralex/Lexapro® (depression), Abilify Maintena® (schizophrenia), Selincro® (alcohol dependence), Azilect® (Parkinson's disease), Xenazine® (chorea associated with Huntington's disease), Sabril® (epilepsy) and Onfi® (Lennox-Gastaut syndrome).

Lundbeck employs approximately 6,000 people worldwide and its products are registered in more than 100 countries. The company has production facilities in China, Denmark, France and Italy and research centers in Denmark, China and the US. Lundbeck generated revenue of approximately DKK 15.3 billion in 2013. The company's market capitalization was around 27 billion DKK (around 3.6 billion EUR) at the end of 2013. Lundbeck is listed on the NASDAQ OMX Copenhagen with a ticker LUN.

Lundbeck employs approximately 6,000 people worldwide and its products are registered in more than 100 countries.

Compared to the real giants of pharma, Lundbeck is a small company in the field. Its MCAP was around 27 billion DKK (around 3.6 billion EUR) at the end of 2013. Lundbeck is listed on Copenhagen.

In its financial guidance for the 2014, Lundbeck expects constant currency revenue to be around DKK 13.5 billion, mainly following depreciation of key exchange rates. The outlook reflects expectations for continued robust performance of the newer product portfolio which partly offsets continued generic erosion, impact from challenging pricing environments and macroeconomic conditions in some major markets. Lundbeck's profit from operations (EBIT) in constant currency is expected to decline to DKK 0.5-1.0 billion in 2014 as a result of increased generic erosion and continued investment in an unprecedented number of product launches and significant costs related to the continued progress of key late-stage clinical development projects.

Lundbeck also stated that it is investing significantly in several new product launches and in its late stage development pipeline, while being in the midst of a transition period. Lundbeck expects to remain profitable in this period with significant growth in the company's newer products offsetting expected revenue decline for some of the mature products.

Compared to the real giants of pharma, Lundbeck is a small company in the field. Lundbeck's MCAP is only 3.6 billion euros, making it a small company compared to the giants in the industry. Despite the relatively small size, typically Lundbeck is considered to be quite conservative in its acquisitions and investments. Lundbeck has also been suffering from the "patent cliff" we have discussed earlier and like we can see from the guidance, the company's profits are expected to decline. Still, we do believe that it has good enough resources to take Selincro forward and it seems to have a strong belief in the drug, making it a good partner to have for Biotie.

We believe that Lundbeck has adequate resources to take Selincro forward and it seems to have a strong belief in the drug, making it a good partner to have for Biotie.

Otsuka Pharmaceutical – Global partner of both Lundbeck and UCB

We are also going to mention Otsuka Pharmaceutical, because it's the global partner both for Lundbeck and UCB. Lundbeck has Otsuka Pharmaceutical products available to the people of 82 countries around the world, and consolidated revenues of more than 12 billion dollars (in fiscal 2012). The market capitalization of Otsuka Holding is around 19 billion dollars.

Otsuka Holdings is a Japan-based pharmaceutical holding company engaged in four business segments. The Medical-related segment is engaged in the sale of ethical drugs, the manufacture, sale and export of curative medicines, as well as the research and development of pharmaceutical products. The Nutraceuticals-related segment is engaged in the manufacture, purchase and sale of nutraceuticals-related products. The Consumer-related segment is engaged in the manufacture and sale of consumer products and mineral water. The Others segment is engaged in the manufacture and sale of chemical products, the manufacture, sale and import of measuring equipment, the manufacture of packaging products, the manufacture of synthetic resin molding products, as well as the storage and handling of its products. As of March 31, 2012, the company had 122 subsidiaries and 33 associated companies.

Otsuka was named as Lundbeck's partner in Japan for Selincro. Close to one million people in Japan have been diagnosed with alcohol dependence, with only 3-6 % currently receiving any kind of treatment. In Japan the medical costs associated with alcohol consumption are estimated at JPY 4 trillion per year. Therefore also the success of Otsuka is at least somehow connected to Biotie.

Otsuka was named as Lundbeck's partner in Japan for Selincro. Close to one million people in Japan have been diagnosed with alcohol dependence, with only 3-6 % currently receiving any kind of treatment. In Japan the medical costs associated with alcohol consumption are estimated at JPY 4 trillion per year.

NIDA (National Institute on Drug Abuse) - nepicastat

NIDA (National Institute on Drug Abuse) is financing the Phase 2 studies of nepicastat. There's also a possibility for further financing, if Phase 2 were to be successful. Biotie holds all the rights to nepicastat and doesn't pay for the development itself, so NIDA could be considered an ideal partner in the development phases.

NIDA's mission is to lead the Nation in bringing the power of science to battle drug abuse and addiction. This charge has two critical components. The first is the strategic support and conduct of research across a broad range of disciplines. The second is ensuring the rapid and effective dissemination and use of the results of that research to significantly improve prevention, treatment and policy as it relates to drug abuse and addiction.

NIDA's funding decisions are based primarily on programmatic priorities of the Institute and scientific merit of the application. Funding strategies for a given year may change depending on priorities within the Institute and those of the NIH.

More information about NIDA can be found at http://www.drugabuse.gov/.

NIDA (National Institute on Drug Abuse) is financing the Phase 2 studies of nepicastat. There's also a possibility for further financing, if Phase 2 would turn out to be a success. Biotie holds all the rights to nepicastat and doesn't pay for the development, so NIDA could be considered an ideal partner in the development phases.

3.3 M&A is one of the keys to success

M&A activity is critical for Biotie in many aspects. First of all, since Biotie doesn't discover the drugs in its product pipeline, it has to acquire them. Most of company's current pipeline comes from the Synosia Therapeutics acquisition. You can identify the development projects coming from Synosia from the product codes: SYN115 (tozadenant), SYN117 and SYN120.

Back then Biotie issued new shares to the shareholders and warrant holders of privately-owned Synosia in an acquisition of the entire issued share capital and outstanding warrants of Synosia. Biotie has disclosed the details of the completion of the transaction as well as a description of the combined entity in a stock exchange release published on 11 January 2011.

In general the success of acquisitions is critical for the long-term success of Biotie. Evaluating the success of the acquisitions is very difficult on short-term, because the development leading to the commercialization takes years.

M&A activity is critical for Biotie in many aspects. First of all, since Biotie doesn't discovery the drugs in its product pipeline, it has to acquire them. Most of company's current pipeline comes from the Synosia Therapeutics acquisition.

Biotie is a likely buyout target in the long run

When thinking about the investment case of Biotie, we believe it's unlikely that the company will stay independent in the long run. It's really rare that a small biotech company develops into a"big pharma" company – it's much more likely that one of the large ones acquires them. Naturally there is a large amount of potential candidates in the biotech industry, but considering the current portfolio one is definitely more likely than the others: Lundbeck.

Lundbeck is already a significant owner of Biotie with a share of 4 %. It is also the most significant partner of Biotie and if Selincro would be highly successful also financially, it would be paying a lot of royalties (and some milestones) to Biotie – possible up to hundreds of millions over the years. Like we already discussed, the maximum milestone payments of Selincro are 89 MEUR, and in addition there would be large amount of royalties that could be much larger than the milestones.

Considering Biotie from the perspective of a possible buyer, we believe that the company could be an excellent buyout target, especially considering its current valuation. Its market capitalization is only roughly 135 MEUR and company has 44 MEUR of cash meaning that company's enterprise value (EV) is less than 100 MEUR. A large pharmaceutical company would also be able to "install" Biotie's product portfolio into their own without significant additional costs, if it would choose to do so. Therefore the extra G&A costs would be minimal, basically they would disappear.

All in all, there's definitely a solid buyout option for the shareholders of Biotie. We aren't suggesting that this would be happening anytime soon. If Lundbeck would be interested in buying Biotie due to Selincro, it would make sense to first see how the sales of the product start to develop. As long as there are no other companies interested in Biotie, Lundbeck doesn't have to make a move. While the valuation is currently low, we do not believe that Lundbeck would be considering the possible acquisition strictly in terms of valuation; it would probably be more interested in the cash flows of Selincro and the potential of the other products.

Biotie is a likely buyout target, if it's successful in the development projects of tozadenant or SYN120. Also if Selincro were to be a large financial success, an acquisition of Biotie would be sensible especially for Lundbeck.

We believe that the company could be an excellent buyout target especially considering its current valuation. Currently Biotie's EV is less than 100 MEUR and the buyer would also be able to "install" Biotie's product portfolio into their own without significant additional costs.

We believe that there's definitely a solid buyout option in Biotie, but we aren't suggesting that this would be happening anytime soon.

4. Outlook for 2014 and our estimates

We must stress once more that Biotie is a long-term case and quarterly results are extremely difficult to estimate and meaningless in the big picture. We have made quarterly estimates for Biotie also, but these are based on assumptions e.g. on timing, which are impossible to estimate accurately. Even the annual results vary greatly due to the timing of large milestone payments. We recommend investors to focus on the progress of development projects, because these are the key to value creation.

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4.1 Company's outlook for 2014 and key upcoming milestones

Biotie's financial guidance for 2014 was the following in the Q4'13 report: "The company expects that both its revenue and research and development expenses will increase during 2014, as a result of milestones that will be received on both tozadenant and Selincro, and the development work that will be performed on tozadenant and SYN120."

Biotie's outlook for 2014 has changed since it published its guidance due to the UCB's decision to return the rights to tozadenant.

However, we believe that this guidance is no longer relevant after UCB's decision to return the rights to tozadenant. Because the situation has changed with tozadenant, the revenue growth is probably out of the question now. After all, prior to the UCB decision, a lot of revenues were expected to come from tozadenant. It's still possible that Biotie finds a new partner that pays a significant up-front payment for the rights already during 2013, but this kind of assumption would not be prudent to make at this point.

Currently the outlook is only relevant for Selincro, nepicastat, BTT-1023 and SYN120.

In addition to the financial guidance, Biotie also gave information on the key upcoming milestones in its 2013 financial statements. We have excluded the one for tozadenant, which is no longer valid, and the one for NRL-1. The ones that are still relevant were the following:

- **Selincro:** Lundbeck will continue the rollout of Selincro in additional European markets into 2014. Biotie is eligible for launch milestones in France, Germany and Spain of 2 MEUR in each market, and further royalties on sales in all markets. Due to the early phase of the launch of Selincro no guidance can be given on expected royalty revenue in 2014. The first clinical Phase 3 study under the joint Lundbeck/Otsuka development program in Japan is expected to be initiated in 2014, but this will not impact Biotie's financial results.

- **Nepicastat (SYN117):** A Phase 2 trial in cocaine dependence, funded by NIDA, is continuing to recruit, and top-line data from the study is currently expected in H1 2015.

- **BTT-1023:** Preparations for a clinical Phase 2 study in primary sclerosing cholangitis are ongoing. The company is in advanced discussions for non-dilutive co-funding for the study.

- **SYN120:** Preparations for a Phase 2 study in Alzheimer's disease have started, with the study expected to begin recruitment by the end of 2014.

Biotie also stated that it will use its financial strength to seek additional pipeline opportunities, including those that it could potentially develop itself through to regulatory approval and beyond. This is company's strategic focus for 2014.

4.2 Our estimates for the coming years

Biotie's revenues are difficult to estimate. Especially their timing for a certain quarter is very challenging, as long as the net sales are strongly dependent on the milestone payments. The cost structure is relatively stable or foreseeable in the short term, because the G&A cost are stable and the R&D projects are known ahead (though the exact costs are difficult to estimate). Fluctuating revenues and the somewhat stable cost structure mean that the profitability will have strong quarterly swings. These are also possible on an annual level, though with more time they should be more stable. Our estimate model is currently based on the following sources for revenue:

MEUR	2014e	2015e	2016e
Revenues	**12.6**	**10.1**	**14.4**
- of which			
Selincro milestones	*6.0*	*4.0*	*3.0*
Selincro royalties	*2.0*	*6.0*	*11.3*
Tozadenant milestones	*4.5*	*0.0*	*0.0*
Nepiscastat with NIDA	*0.0*	*0.0*	*0.0*
Others	*0.1*	*0.1*	*0.1*

Table 8. *Estimated revenues of Biotie.* *Source: Inderes*

These revenues do not include anything that would come from new agreements, e.g. possible payments for tozadenant. The easiest revenues to estimate on an annual level are the milestone payments of 6 MEUR; Lundbeck has announced its plan to launch Selincro in France, Germany and Spain during 2014. This is a significant revenue for Biotie in the short term. In 2015 the ramp-up in Europe should progress further, and some milestone payments can be expected also then.

Royalties for Selincro should clearly grow in 2014, when Lundbeck is launching the product in more markets. Also the actual usage of the product should grow with the awareness. Still the sales of Selincro are expected to be modest in the coming years, so royalties shouldn't be a huge contributor to the revenues of Biotie soon. We are currently expecting the royalties to be around 2 MEUR in 2014 and possible roughly 6 MEUR in 2015.

Other milestones could be significant, if a new partner for tozadenant is found during 2014. Depending on the terms of the agreement, it could include a significant up-front payment. However, we haven't taken this into account for now. The only revenues that we are currently expecting from tozadenant are the payments that still should come from UCB. There should be some millions of euros "pending" from the costs included in the old contract that UCB should cover. We are currently estimating all of these to be around 4.5 MEUR in 2014, possible slightly more. Biotie is progressing with SYN120 on its own, so there shouldn't be any income deriving from that before the next phase.

The other side is naturally the cost structure, which could be simplified to include the following:

MEUR	2014e	2015e	2016e
Gross profit	**12.6**	**10.1**	**14.4**
R&D expenses	**8.3**	**12.0**	**12.0**
Tozadenant	*3.5*	*0.0*	*0.0*
Nepicastat	*0.0*	*0.0*	*0.0*
SYN120	*4.0*	*12.0*	*12.0*
VAP-1	*0.8*	*0.0*	*0.0*
Selincro	*0.0*	*0.0*	*0.0*
G&A expenses	**8.0**	**8.4**	**8.8**
Costs total	**16.3**	**20.4**	**20.8**

Table 9. *Estimated costs of Biotie.* *Source: Inderes*

Also in the cost side we have included only those that should come from the already published plans. The most significant R&D costs should be the Phase 2 trials of SYN120 that should start in H2'14. We have allocated 4 MEUR of R&D costs to this project in 2014 and 12 MEUR both in 2015 and 2016. The total cost of SYN120 Phase 2 program should be around 25-30 MEUR. Like discussed, this is probably the most important investment of Biotie in the coming years.

Biotie's revenues are still mostly milestone driven, which means that the income can fluctuate strongly on quarterly or even on annual level. This can change in the coming years, if Selincro's royalties become more dominant.

Currently Biotie's main income sources are Selincro milestones, Selincro royalties and other milestones (the most relevant is tozadenant). Our estimates do not include any large payments that would come from new agreements.

In 2014 Biotie should receive 6 MEUR in milestone payments, when Selincro is launched in France, Germany and Spain. Royalties for Selincro should clearly grow.

Other milestones could be significant, if a new partner for tozadenant is found during 2014. Depending on the terms of the agreement, it could include a significant up-front payment.

Biotie should receive some minor payments (few million euros) from UCB under the terms of its old contract in 2014.

The most significant R&D costs should be the Phase 2 trials of SYN120 that should start in H2'14. We have allocated 4 MEUR of R&D costs for this project in 2014 and 12 MEUR both in 2015 and 2016.

The total cost of SYN120 Phase 2 program should be around 25-30 MEUR.

The General and Administrative (G&A) expenses are also significant for Biotie. Expenditures related to the day-to-day operations of a business; items like rent, utilities, insurance and managerial salaries. These have typically been around 7-8 MEUR. We currently expect them to be 8 MEUR in 2014 and grow with a pace of roughly 5 % after this. The "inflation" is expected to derive from the revised strategy (possible adding some resources) and the positive development of Biotie's product pipeline. However, if development projects would be discontinued (e.g. as a result of negative data), we would expect the company to also cut G&A expenses.

Since we do not believe that Biotie would be progressing to Phase 3 with tozadenant without a partner, we have allocated only some minor costs from the project in 2014. Most of these should be covered by UCB, so tozadenant shouldn't have a significant effect on the earnings of Biotie in 2014.

We believe that the earnings of Biotie will be in the red, if there are no significant payments from tozadenant (or the others) this year. We are currently expecting the costs to be around 16 MEUR this year, increasing to over 20 MEUR in 2015. We are expecting the revenues to be around 12 MEUR in both 2014 and in 2015, so we are expecting FY'14 earnings to be -4 MEUR and FY'15 around -8 MEUR. In the past there have been many years when Biotie has had practically no revenues and still it has been investing heavily in the development projects. Investors need to remember the earnings logic of biotech companies - P&L often tells more about the current situation of development projects than the direction that the company's earnings are heading in the long term.

The most important conclusion on the earnings estimates for the next few years is the following: if our estimates are correct, Biotie can make the planned investments to SYN120 without hurting its balance sheet significantly. Like discussed, the company has around 44 MEUR of cash on its balance sheet, so it could carry losses we are projecting now without problems. In general investors can assume the cash flows to be more or less in-line with the P&L. The situation would be different if Biotie would be forced to make significant investments into tozadenant (without a partner), develop BTT-1023 with its own money or acquire some other assets.

P&L Statement (MEUR)	2014e	2015e	2016e
Revenues	**12.6**	**10.1**	**14.4**
- of which			
Selincro milestones	*6.0*	*4.0*	*3.0*
Selincro royalties	*2.0*	*6.0*	*11.3*
Tozadenant milestones	*4.5*	*0.0*	*0.0*
Nepiscastat with NIDA	*0.0*	*0.0*	*0.0*
Others	*0.1*	*0.1*	*0.1*
Cost structure			
Gross profit	**12.6**	**10.1**	**14.4**
R&D expenses	**8.3**	**12.0**	**12.0**
Tozadenant	*3.5*	*0.0*	*0.0*
Nepicastat	*0.0*	*0.0*	*0.0*
SYN120	*4.0*	*12.0*	*12.0*
VAP-1	*0.8*	*0.0*	*0.0*
Selincro	*0.0*	*0.0*	*0.0*
G&A expenses	**8.0**	**8.4**	**8.8**
Costs total	**16.3**	**20.4**	**20.8**
Adjusted EBIT	**-3.7**	**-10.2**	**-6.4**
Net interest	0.0	0.0	0.0
Pre-tax profit	**-3.7**	**-10.2**	**-6.4**
Taxes	0.0	0.0	0.0
Adjusted net earnings	**-3.7**	**-10.2**	**-6.4**

Table 10. *Estimated revenues of Biotie.* *Source: Inderes*

G&A expenses have typically been around 7-8 MEUR annually. We currently expect them to be 8 MEUR in 2014 and grow with a pace of roughly 5 % after this.

Since we do not believe that Biotie would be progressing to Phase 3 with tozadenant without a partner, we have allocated only some minor costs from the project in 2014.

We believe that the FY'14 earnings of Biotie will be clearly in the red, if there are no significant payments from tozadenant. Without new developments, the cash flow will be negative in the coming years as the revenues cannot carry the investments into SYN120 fully.

Still, if our estimates are correct, Biotie can make the planned investments to SYN120 without hurting its balance sheet significantly. The situation would be different, if Biotie would make significant investments into other assets.

4.3 Assumptions behind the estimates

There are plenty of assumptions that we have been forced to make in order to create a base scenario as well as our estimates. We have already explained the assumptions that we have made with the key products, but here are some more in general. All our estimates are based on assumptions that mostly concern the development phases and their financing. We are currently assuming that:

- Biotie will finance Phase 2 of SYN120 and it will cost around 25-30 MEUR
- Biotie will not make significant investment to tozadenant without a partner
- Biotie will not make significant investment to BTT-1023 without outside funding
- NIDA will cover the cost of nepicastat
- NRL-1 option isn't used
- Selincro progresses in Europe as Lundbeck has planned (Japan not included in our estimates)

When the partnering situation of tozadenant will be resolved, we'll update our estimates accordingly. Most likely this decision will also affect our view on the value of tozadenant. The same goes also with other new information, such as the Phase 2 results of nepicastat. Our estimates naturally do not include any M&A activity; they are based on the current structure and product portfolio of the company.

There are many different possibilities for Biotie and we have made assumptions on which choices they'll make in order to create sensible valuation model.

Eventually the decisions of Biotie should be driven by shareholder value optimization (also taking risk/return-ratio into account).

5. Valuation of Biotie

Biotech companies cannot be valued with the traditional multiples like P/E, EV/EBIT or P/B. The company could be doing valuable development for 10-15 years before seeing any cash flow from the process (assuming no partnering and milestone payments). With the multiples approach the product wouldn't have any value prior to the launch, very low value when it's ramping up sales and extremely high value during the peak sales period – just before the product protection ends and the value of the product is mostly likely going to be dramatically lower.

Biotech companies are typically valued based on the value of the product portfolio. The products are value with risk-adjusted net present value (rNPV).

DCF valuation is also very challenging, since there are specific timelines to this also. Typically the cash flows are expected to end with the protection, at least when it comes to royalties. Therefore the terminal value, which is critical in a normal DCF model, could be considered to be zero. If the company has only a few products, like Biotie, there are huge swings with the result as well as cash flow. This is not easy to model and it is far from ideal when it comes to the DCF. Also the very high uncertainty is now captured through this model.

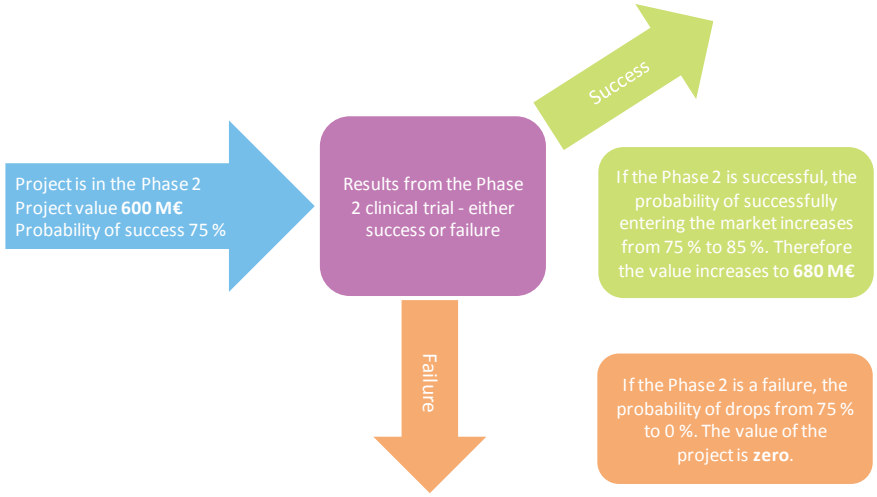
rNPV modifies the standard NPV calculation of discounted cash flow (DCF) analysis by adjusting each cash flow by the estimated probability that it occurs.

Typically biotech companies are valued based on the value of the product portfolio. The products are valued with risk-adjusted net present value (rNPV). rNPV modifies the standard NPV calculation of discounted cash flow (DCF) analysis by adjusting (multiplying) each cash flow by the estimated probability that it occurs (the estimated success rate). In the language of probability theory, the rNPV is the expected value. Alternative methods can be built around decision three and option pricing theories, but we believe the rNPV method to be the best practice currently. Therefore we are using it to value Biotie.

One significant problem with the biotech products is that their whole value can basically disappear overnight – and often this is the case, since so many fail. A potential blockbuster drug can be valued up to a billion dollars, but its value can drop to zero after the negative results e.g. from Phase 3 studies. An otherwise perfect drug can have one really dangerous side-effect found at the last minute, and if the situation cannot be corrected, its value can be zero. If a company has invested a billion euros into the development prior to this, it's all gone at this point. The estimated value always depends on the market potential as well as the probability of successful launch to the markets. The "checkpoint" of this probability (%) is typically after each development phase, and therefore the results always change the value of the product. We have explained this with the following example.

The estimated value always depends on the market potential as well as the probability of successful launch to the markets. The "checkpoint" of this probability (%) is typically after each development phase, and therefore the results always change the value of the product.

These are the critical value infliction points that we have been discussing throughout the report.



Graph 8. The value of a development project is tight to the probability of successful launch. The knotpoints of the project are critical. *Source: Inderes*

It's natural that the investment decisions are always made with imperfect information, though it's the best that is available at the time. This leads to a situation, where a products NPV could be negative at a certain point of time (the odds are against you, but you do not know it). Naturally these investments shouldn't be made, but also the management can make wrong decisions and push forward without positive rNPV due to different assumptions. We have discussed the role of management earlier in chapter 1.6.

5.1 Valuing the current product portfolio

Biotie's products are in different development phases, have different strengths and weaknesses and their market potentials vary greatly. Therefore they must be valued separately, which we have done in the following chapters. Our focus naturally is on the most valued products and those near the value infliction points, because they are the ones that will drive the market value of Biotie. We have made estimates also for the others, where at least the status of the development is clear. Some of these include very rough assumptions, so we recommend investors to consider them only as rough guidelines of the values.

We focus on the most valued products and those near the value infliction points, because they are the ones that will drive the market value of Biotie.

Product	Status	Probability of success (%)	Estimated launch year	Estimated peak market share	Estimated royalty	Estimated peak sales	Patent expiry	Estimated value (rNPV)
Selincro (nalmefene) *Alcohol dependence*	Approved and launched in EU	75 % regarding commercial success	Launched in 2013	33 %	15 %	300 MEUR	2023	88 MEUR
Tozadenant (SYN115) *Parkinson's disease*	Phase 3-ready	Possible 30 % (partnering, clinical & commercial risks)	2020	Possible significant in terms of value	10 %	Easily higher than billion euros, if the profile is favorable	2031	47 MEUR
SYN120 - *Alzheimer's disease and other cognitive disorders.*	Phase 2-ready	Around 20 % (clinical, financial & commercial risks)	2020	Small - lots of competitors	12 %	Huge market potential	2030	25 MEUR
Nepicastat (SYN117) - *Cocaine dependence*	Phase 2 ongoing	5 %, very high risk due to the difficult target group	2020	So far no competitors	Possibility of independent launch	Small market, difficult to estimate	Unknown at this point	5 MEUR
BTT-1023 (VAP-1 antibody) *Fibrosis*	Phase 2-ready	10 %, still early in the pipeline	Will be evaluated after financing P2	Possible orphan medinicine	Too early to estimate	Small market, but possible high share	Unknown at this point	Value cannot be determined at this point
NRL-1 - option *Acute Repetitive Epileptic Seizures*	Phase 2-ready	0 %	Biotie didn't use the buy option	-	-	-	-	No value at this point

Table 1. *Biotie valuation model and key assumptions.* *Source: Inderes*

Some points have been left open at the moment, because there isn't enough information available in order to make educated assumptions. For example there are different protection forms (patent expiry) and some of them are related to the timing of the launch as well as the status of the medicine. Many estimates have to be made so far into the future that their accuracy is doubtful at best. Once again, it's more important to see how these values develop over time when more data is gathered.

5.2 Consolidating the value to the group level

The value of the product portfolio gives the basis for the valuation. However, it doesn't directly represent the value of the company to the shareholders. In order to consolidate the value to the group level, we have to add the gross cash, eliminate the effect of G&A costs that haven't been included in the values of the products and considering the debts of the company.

The value of the product portfolio is the basis for the valuation, but it doesn't directly represent the value of the company for the shareholders. In order to do this we need to adjust the value for G&A costs and cash (or debt) balance.

We have made very cautious estimates when it comes to the value of Biotie. E.g. if the development process of tozadenant is successful, the value goes up significantly.

Consolidating the value	NPV	Explanation
rNPV of the product porftolio	165 MEUR	See table above
G&A costs	-64 MEUR	Cost of doing business that is eliminated from the value of product portfolio
Gross cash	44 MEUR	Note that company has liabilities from TEKES, payble if profitable (not included here)
Total value	146 MEUR	Value according to our risk-adjusted net presented value model
Value per share	0.32 EUR	We have used the fully diluted number of shares

Table 11. *Biotie valuation model and key assumptions.* *Source: Inderes*

In general we would like to point out that we have made very cautious estimates when it comes to the value of Biotie. If the development project of tozadenant is successful, the value goes up significantly. We tried to be cautious also when it comes to the success probabilities of different products in the development.

When consolidating the value of the product portfolio we need to eliminate the G&A costs of the group. This is the cost of doing business, and we have estimated it to be 8 MEUR in 2014. We have estimated the inflation of G&A cost to be 5 % annually, which is very high and takes into account the evolving strategy of Biotie. We hope that the actual cost inflation wouldn't be quite this high. The elimination of G&A costs from the value of Biotie means a deduction of 65 MEUR with these assumptions.

We have estimated the inflation of G&A cost to be 5 % annually, which is very high and takes into account the evolving strategy of Biotie.

At the end of 2013 Biotie had 43.7 MEUR cash on its balance sheet, which is added to the value. The company also had around 20 MEUR of debt, which would typically be discounted from the value. However, mostly of these debts are from TEKES and Biotie doesn't have to pay back capital loans from the Tekes for a long time. The Tekes non-convertible loans have interest and capital that are only repayable if the company has sufficient funds within the group as a whole for profit distribution, which would mean that they become payable only after Biotie has made roughly 90 MEUR of net earnings. Even in the best case scenario, this would take years – and when thinking about the valuation, the share price would definitely be at a completely new level if this would happen. At the end of 2013 Biotie's balance sheet had 16.3 MEUR of non-convertible capital loans from Tekes as well as 2.7 MEUR of long-term R&D loans from Tekes. In addition, it had convertible capital loans amounting to 1.7 MEUR, which we have taken into account in the dilution of the share. Based on these points, we believe that the debt can be excluded from the value.

Biotie's debt is mostly from TEKES and it has to be paid back only if the company has sufficient funds within the group as a whole for profit distribution. If this would happen anytime soon, all the shareholders would certainly be happy. Therefore we have excluded them from the fair value.

After all the adjustments, we determine the value of Biotie to be around 165 MEUR currently. The company's fully diluted number of shares is around 460 million (assuming dilution effect of roughly 5 % from the current). Therefore we believe the value of Biotie's share to be around 0.32 EUR.

We are currently using a high WACC of 16 %

One of the key elements in the valuation is the used discount factor (WACC, Weighted Average Cost of Capital). We have used a very high WACC of 16 % due to the company's high risk profile. When looking at the studies made on the WACC-rates used in biotechnology, it is around 15 % for small biotech companies. However, the risk profile of Biotie is becoming lower as the royalties of Selincro start ramping up. The cash burn rate is relatively low, and since the company's income is growing significantly in the future, its financial position is getting stronger. Therefore it might be justified to use a lower WACC in the future, when the Selincro royalties become a larger part of the financing.

One of the key elements in the valuation is the used discount factor (WACC). We have used a very high WACC of 16 % due to the company's high risk profile.

The risk profile of Biotie lowers as the royalties of Selincro start ramping up. Cash burn rate is currently low and the financial situation solid.

Tax rate, WACC	20 %
Target debt ratio D/(D+E)	0.0 %
Cost of debt	6.0 %
Equity beta	1.75
Market risk premium	6.0 %
Liquidity premium	1.5 %
Riskfree interest rate	4.0 %
Cost of equity	16.0 %
WACC	16.0 %

Table 12. *Assumptions behind WACC.* *Source: Inderes*

Also it's important to notice that Biotie is currently carrying only a small portion of its R&D costs by itself, but this situation might change like we have discussed. The biggest R&D investments of Biotie will be made to SYN120 in the coming years. We aren't expecting Biotie to make significant investments into tozadenant without a partner; if this assumption would change, the situation would be greatly different. At least the Phase 2 studies of nepicastat are financed by NIDA, so Biotie doesn't carry the downside risks of the development, but it still has the upside potential.

Biotie is currently carrying only a small portion of its R&D costs by itself. Biotie's biggest R&D investments will be made to SYN120 in the coming years. We aren't expecting Biotie to make significant investments into tozadenant without a partner; if this assumption would change, the situation would be greatly different.

All in all, we believe that Biotie's risks are under control in the coming years. Therefore the high WACC used in the valuation reflects specifically the very high risks in general in the biotech sector, as well as our will to be cautious in our estimates that are very uncertain due to the very long timeline of the development projects.

5.3 Sensitivity analysis

When it comes to a company like Biotie, there are always a lot of uncertainties in valuation. Mostly these are regarding the assumptions that have to be made in the process. Because these can never be exactly correct, it's important to determine how much the value would be if some of the assumptions would be changed.

Here we are presenting some of the key sensitivities that we have demonstrated with Selincro and tozadenant; naturally similar ones could be done also with the others, but the main point is to understand the dynamics of valuation. We believe these are sufficient to accomplish this.

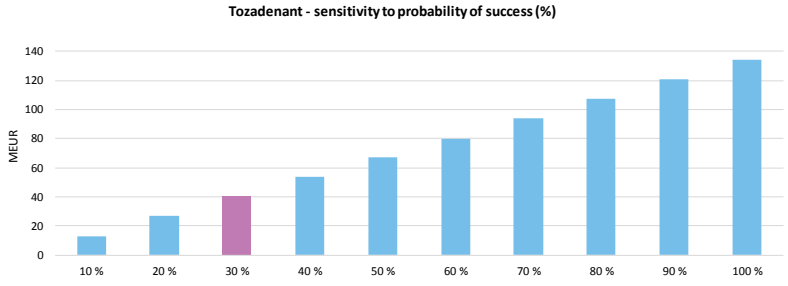
There are always a lot of uncertainties in valuation. The assumptions that have to be made can never be exactly correct, it's important to determine how much the value would be if some of the assumptions would be changed.

Here we have shown how the values of products would change, if we would change the 1) probability of success (%) and 2) level of royalties.

When it comes to value, the most significant is the probability of success. This is especially true when it comes to tozadenant.

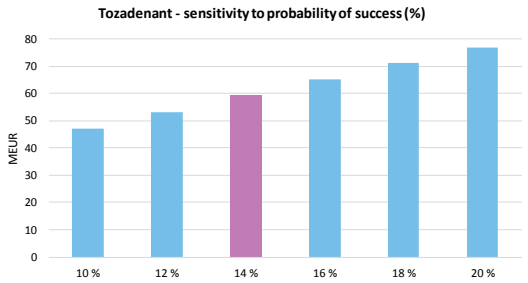
Sensitivity analysis	Probability of success (%) and value in MEUR									
Product	10 %	20 %	30 %	40 %	50 %	60 %	70 %	80 %	90 %	100 %
Selincro	10	20	29	39	49	59	69	78	105	117
Tozadenant	13	27	40	54	67	80	94	107	121	134

Table 7. Sensitivity analysis: changing the probability of success (%) *Source: Inderes*



Sensitivity analysis	Level of royalties (%) and value in MEUR					
Product	10 %	12 %	14 %	16 %	18 %	20 %
Selincro	68	78	87	97	107	117
Tozadenant	47	53	59	65	71	77

Table 8. Sensitivity analysis: changing the probability of success (%) *Source: Inderes*



6. Risks

We have been writing about the high risks of biotechnology throughout this report. In this chapter we aim to summarize the biggest risks of the business, as well as those concerning Biotie. However, we have already mentioned the biggest risks regarding the development many times (i.e. uncertainties related to drug development and regulatory clearance). The amount of revenues derived from licensing or collaborative development contracts will depend on a number of unpredictable factors and as a result, Biotie's revenues may fluctuate materially on a monthly, semiannual and annual basis.

Biotech is a high risk business. Uncertainties related to drug development and regulatory clearances together with high costs of the development process are undeniable.

Also it should be clear at this point that the competition is always a risk. As competitors develop their technologies, they may develop proprietary positions in certain areas that may have a material adverse effect on the competitiveness of Biotie's products on the market.

Still, the risks also have a different side: high upside if things develop favorable. These should be in balance if the analysis is done correctly.

While we have been discussing the high risk profile of Biotie at length, we believe it's only fair to also consider mitigating factors that there are. The company has a portfolio of products in different stages and for different diseases, so it's not a one trick pony like many in this industry. Biotie also has the ability to cut costs relatively quickly in a negative scenario, and it also has a strong cash position. Comparing Biotie to a "typical" small cap biotech company, we believe it is significantly less risky. Biotie's future is not controlled by the success of an individual project.

While the risk profile of Biotie is undeniable high, we believe that it is low compared to other companies with similar profile in general.

Still, biotech is a high risk business. The other side of the coin is the huge potential upside, if things develop favorable. The basic nature of the business is that one highly successful product generates enough cash flow to pay for all the failed ones. If all the risks are accounted for correctly, the risk and reward are in balance.

6.1 General risks of Biotie and other biotechnology companies

These are some of the general risks that should be considered when investing in a biotech company.

Development stage of the products, commercialization and market acceptance

Biotie's ability to achieve positive results depends on whether Biotie or its partners successfully complete the development of its present and future product candidates into marketable products, enter into collaboration agreements, obtain regulatory approvals, and establish sales and marketing agreements with third parties. Biotie's operations and financial condition are partly dependent on finding suitable licensing collaborators, and on the consideration that Biotie receives from commercialization agreements. So far Biotie has only been able to launch Selincro with its partners, but it needs a lot more in order to make consistent profits. Even at this point Biotie's ability to generate any significant revenue depends on the acceptance of the products by medical authorities, physicians and patients.

In addition to the "scientific" risks related to developing new products, there's always a commercial risk also.

Intellectual property rights

Like discussed earlier, this business is all about the IPR. Since the value depends on the rights, there are also major risks regarding their correct handling. Failures in obtaining, managing and protecting intellectual property rights could have a material adverse effect on Biotie's business, results of operations and financial condition. There can be no assurance that Biotie's product candidates, technologies, processes or their application do not currently or will not in the future infringe the patents or other proprietary rights of third parties.

Biotech is an IPR business and there are always certain risks related to them.

Adequacy financing and future capital needs

The amount or accrual of Biotie's expenditures will depend on the progress of the continuing research and development activities and the expenditure relating thereto. Additional equity and/or

The financing risk of Biotie is currently relatively small, but

debt financing of the company will be an essential element in securing the financial basis needed to continue business operations. Because the financial position of Biotie is currently strong, we do not see this is as a significant risk at the moment.

the situation could change in the future.

Collaboration agreements

There can be no assurances that Biotie will be able to establish additional collaboration agreements and that such agreements will be on terms favorable to Biotie. Collaboration is still critical for a small company like Biotie, even with the evolved strategy. While we do not see the partnering situation of Biotie as actually difficult per se, the terms of these contracts are always a significant risk that the company has to carry. Financial terms like royalties and milestone payment are all factors in these contracts and depend on the bargaining power of the parties. This always represents risks for Biotie.

While finding a partner should be relatively easy, finding the best possible partner with attractive terms for Biotie is always a difficult task.

Product liability and insurance

Biotie may be subject to the risk of product liability claims alleging adverse effects caused by use of Biotie's products. Any such claim could result in substantial liability to the company, including compensatory and punitive damages. This is unlikely due to the tight scrutiny in the development process, but if there would be problems, they could be significant.

Product liability should be afar-fetched risk for Biotie, but it's still possible.

Pricing and reimbursement of pharmaceutical products

The pricing and reimbursement of pharmaceutical products is dependent on the applicable price and reimbursement regulations and these factors could have a material adverse effect on Biotie's business, result of operations and financial condition.

Reimbursement decisions and pricing are always important when it comes to financial success.

Risks relating to the balance sheet position

Biotie's intangible assets and goodwill are tested for impairment annually and whenever there is an indication that an asset may be impaired. Should it be required to recognize impairments due to the impairment testing, it could have a material negative effect on the company's results and balance sheet position, albeit they would be non-cash in nature.

Possible intangible asset impairments could hurt the balance sheet of Biotie.

6.2 Biotie's risk profile is high

While all the risks mentioned above also apply to Biotie in some degree, the company also has some more specific and relevant risks. In this chapter we try to demonstrate some of the most important ones.

The new strategy

Biotie's recent change in strategy brings more potential, but it also brings different kinds of risks. The company doesn't have experience in launching, marketing or selling products independently. In the biotech industry one of the key factors are regulation, pricing and creating acceptance for the treatment. The financial risks are the highest in the latter phases. This could be a major risk, if the company actually attempts to facilitate the new strategy with a "wrong product".

If the management were to make strategic mistakes, it could be very harmful for investors.

M&A

Mergers and acquisitions (M&A) are one of keys for Biotie's success like we discussed earlier. However, they are always risky. M&A is critical for the pipeline and even though the business has relatively good visibility like discussed, the information is hardly ever completely identical on the both sides of the table. Biotie often uses its own shares as well as options as payment, so unsuccessful acquisitions could also create a lot of dilution (see the next point).

M&A is critical for Biotie, but due to the always asymmetric information, it's also always a risk.

Dilution of the shareholding

Biotie has currently three option plans: the Swiss option plan, the Stock Option Plan 2011 and the Stock Option Plan 2014. In addition it has two incentive plans that could also dilute the number of shares (Equity Incentive Plan and Equity Incentive Plan 2014). As a whole there are a potential maximum of roughly 31 million shares that could be issued to employees if they are (1) issued in the first place; and (2) the employees to whom they are issued stay for the required amount of time (2 or 3 years depending on the program). Note that this would be the absolute maximum, which is extremely unlikely to happen.

In addition there are a potential maximum of 6,840,000 additional shares that could be issued if (1) the share price grows by at least 100 % from 1 January 2014 to 31 December 2016; and (2) if those employees are still with the company at 31 December 2016. We do not see this as a problematic program for the shareholders, since the share price would have risen very substantially before the dilution becomes significant. The share price was 0.28 euros at the end of 2013.

Detailed information about the option plans can be found at www.biotie.com.

Biotie has many different option and incentive plans that are likely to increase the number of share in the future. The maximum dilution of all these programs is around 8.4 %, if we use 456 million shares as a comparison point.

The actual dilution is likely to be much lower, but it could still be significant (possible around 3-5 %).

Appendix I - Basics of medicine development

Different stages of the development process

We have collected some general information about the drug development process. The main source has been the FDA, but there's also some information from Orion.

If we look at the big picture, the whole chain drug development process includes the following:

- Non-clinical research
- Clinical studies
- Product development
- Biostatistics
- Regulatory affairs
- Drug safety

Different phases of the development process can be divided into smaller parts, but we believe that our interests can be satisfied with the basic knowledge of the whole process. After this, we will focus more on the areas where Biotie is most active – the clinical studies including Phases 1-3.

Picture 3. *Research and development of medicine.* *Source: Orion*

Non-clinical Research

Discovery of a new drug candidate is a long iterative process, where properties of molecules are improved systematically. The number of theoretically possible structures to be synthesized is unlimited - but what is actually synthesized depends on careful selection and structural design. In the beginning of a new project, scientists are searching for compounds suitable for chemical optimization of desired properties. In silico virtual screening methods are utilized in the search of so-called Hit structures. Creation of Structure Activity Relationships (SAR) will be possible after suitable experimental data related to structures have been obtained. SARs guide structural design of the new structures to be synthesized.

Many properties are already acceptable for a lead compound, but they still need to be optimized. During the optimization, scientists have to improve many important properties of the compounds in addition to the biological activity, e.g. absorption, distribution, metabolism, excretion and safety parameters. With further optimization it is ensured that efficacy, kinetics and safety of a new chemical entity fulfil requirements of a drug candidate.

As a final outcome of the optimization process usually only one drug candidate will be selected for further development and clinical studies, where the final proof of concept as well as feasibility will be tested. In these studies, new molecular biology methods are applied to identify biological markers (biomarkers) that enable deeper understanding of molecular level changes in drug action and thus improve the prediction of efficacy and safety at earlier development phases.

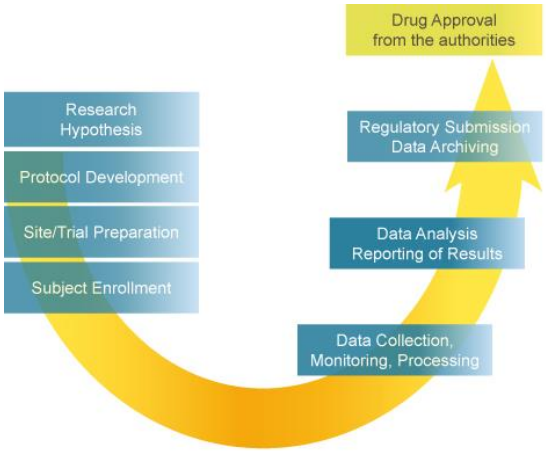
During the non-clinical research you want to clarify:

- What kind of medicine could help in the illness, where there is a need for new efficient and safe treatment?
- What kind of molecule could help and be safe, and can a drug product be developed from it?
- Do the results of the experiments allow that the medicine can be administered to humans?

Clinical Studies

In the clinical development phase the aim is to prove the safety and efficacy of the drug in humans. Clinical studies are divided into Phases I-IV during the progress of the development program. Studies can be conducted in healthy volunteers and in volunteer patient populations - the participation of study subjects in clinical studies is always confidential and the subject can discontinue the participation any time.

The procedures of clinical studies are carefully designed. The process is strictly regulated by the authorities and the studies are carried out in the same way with any products:



Graph 8. *Drug development process.* *Source: Orion*

Before a clinical study can be started, a favorable opinion on the study protocol and associated documents has to be obtained from an ethics committee, and the national medicines agency of the country must approve the study. The agency also supervises the progression of the clinical study. When the clinical study is completed, a report on the results and study conduct will be submitted to the agency.

Clinical Phase I

During Phase 1 studies, researchers test a new drug in normal volunteers (healthy people). In most cases, 20 to 80 healthy volunteers participate in Phase 1. However, if a new drug is intended for use in cancer patients, researchers conduct Phase 1 studies in patients with that type of cancer. Phase 1 studies are closely monitored and gather information about how a drug interacts with the human body. Researchers adjust dosing schemes based on animal data to find out how much of a drug the body can tolerate and what its acute side effects are.

As a Phase 1 trial continues, researchers answer research questions related to how it works in the body, the side effects associated with increased dosage, and early information about how effective it is to determine how best to administer the drug to limit risks and maximize possible benefits. This is important to the design of Phase 2 studies.

During Phase I you want to clarify:

- How does the drug move and get to the correct target in the body?
- What doses a person can take and what effects are expected?
- For how long the drug has effect and how it is metabolized and excreted from the body?

Clinical Phase II

In the clinical Phase II-studies the medicine is given to patients and its effects in the illness are investigated (Proof-of-concept) and the effective doses are selected. In the studies carried out with dozens of patients in clinics and hospitals, the aim is to further confirm the effects of the medication in the body and to get hints of efficacy. During the studies a lot of information is gained to plan adequate Phase III trials with proper design. The duration of Phase II depends on the indication and on how quickly the effect of the medicine can be seen and measured.

Typically involving a few hundred patients, these studies aren't large enough to show whether the drug will be beneficial. Instead, Phase 2 studies provide researchers with additional safety data. Researchers use these data to refine research questions, develop research methods, and design new Phase 3 research protocols.

In Phase II you want to clarify:

- How does the medicine effect the illness?
- Are the expected signs of efficacy seen in patients?
- Which doses are needed to get the desired effect without adverse effects?

Late development - Clinical Phase III

In Phase III-studies the efficacy and safety of the medicine are confirmed with even thousands of patients in clinics and hospitals in several countries. The studies are blinded so that the patients, their doctors or the company representatives do not know which patient is getting the investigational medicine and who is getting placebo or the already marketed reference medicine.

Phase III is the largest and most expensive part of the development - the costs cover about two thirds of the whole development cost of a new proprietary product. The strategy of Biotie is that in this Phase they work closely with our partners to share the costs and risks.

Sometimes known as pivotal studies, these studies involve 300 to 3,000 participants. Phase 3 studies provide most of the safety data. In previous studies, it is possible that less common side effects might have gone undetected. Because these studies are larger and longer in duration, the results are more likely to show long-term or rare side effects.

After the Phase III studies, all the results obtained during development are compiled together and a marketing authorisation application is prepared. After the marketing authorisation, often Phase IV-studies are carried out to continue collecting information on the medicine in the markets.

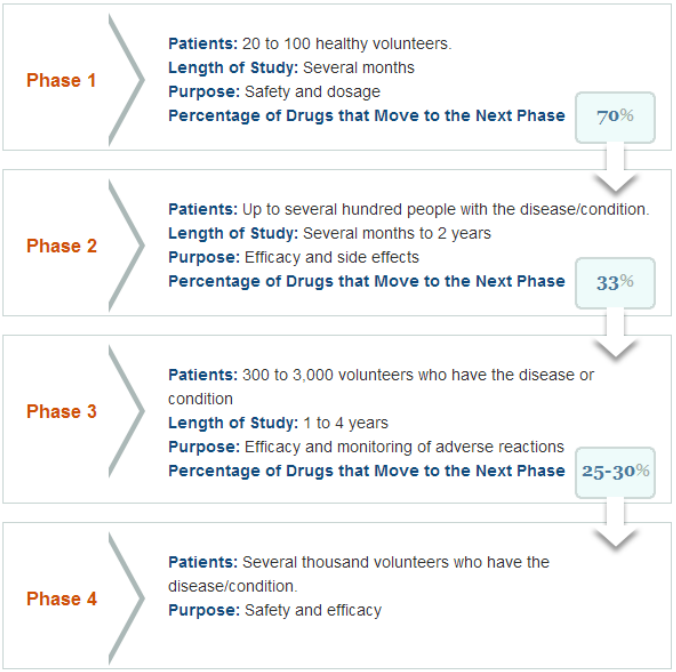
During the Phase III you want to clarify:

- Can we repeat the results we have seen with the medicine earlier on in regards to efficacy and safety in large patient groups?
- Are the chosen doses effective and safe?

Average success rates of different phases

In the following graph you can see the FDA data for the success rates of different clinical phases. The FDA data is naturally from the United States market, but the success rates are somewhat similar to those in Europe (under EMA) and Japan. This rates show what we mean when we are talking about biotechnology as a risky business. The large majority of development processes fail at some point. Investors need to also remember that development costs are high and that the commercial success is far from guaranteed, even if the medicine is launched to the markets.

The graph also includes the most important data of the process and therefore is a good summary for the development process.



Picture 4. *Key elements of the clinical drug development.* *Source: FDA*

EMA / FDA review

If a drug developer has evidence from its early tests and preclinical and clinical research that a drug is safe and effective for its intended use, the company can file an application to market the drug. The FDA review team thoroughly examines all submitted data on the drug and, makes a decision to approve or not to approve it.

A New Drug Application (NDA) tells the full story of a drug. Its purpose is to demonstrate that a drug is safe and effective for its intended use in the population studied. A drug developer must include everything about a drug—from preclinical data to Phase 3 trial data—in an NDA. Developers must include reports on all studies, data, and analyses. Once the FDA receives an NDA, the review team decides if it is complete. If it is, the review team has 6 to 10 months to make a decision on whether to approve the drug.

ERA / FDA Approval

In cases where the FDA determines that a drug has been shown to be safe and effective for its intended use, it is then necessary to work with the applicant to develop and refine prescribing information. This is referred to as “labeling.” Labeling accurately and objectively describes the basis for approval and how best to use the drug. Often remaining issues need to be resolved before the drug can be approved for marketing. Sometimes the FDA requires the developer to address questions based on existing data. In other cases, the FDA requires additional studies. At this point, the developer can decide whether or not to continue further development. If a developer disagrees with an FDA decision, there are mechanisms for formal appeal.

Post-Market Safety Monitoring

Even though clinical trials provide important information on a drug’s efficacy and safety, it is impossible to have complete information about the safety of a drug at the time of approval. Despite the rigorous steps in the process of drug development, limitations exist. Therefore, the true picture of a product’s safety actually evolves over the months and even years that make up a product’s lifetime in the marketplace. The FDA reviews reports of problems with prescription and over-the-counter drugs, and can decide to add cautions to the dosage or usage information, as well as other measures for more serious issues.

Appendix II - Additional information on Parkinson's disease

Parkinson's disease: the current medications and treatments

There are many medications available to treat the symptoms of Parkinson's, although none yet that actually reverse the effects of the disease. It is common for people with PD to take a variety of these medications – all at different doses and at different times of day - in order to manage the symptoms of the disease. While keeping track of medications can be a challenging task, understanding your medications and sticking to a schedule will provide the greatest benefit from the drugs and avoid unpleasant "off" periods due to missed doses. Note that we have included here only the most commonly used medications. The source of the following information is Parkinson's Disease Foundation (PDF).

Class/Type and Medications	How It Works	What To Know	Potential Side Effects
Levodopa Carbidopa/Levodopa (Sinemet®) Carbidopa/Levodopa controlled release (Sinemet CR®) Carbidopa/Levodopa orally disintegrating tablet (Parcopa®) Carbidopa/Levodopa/ Entacapone (Stalevo®)	Levodopa is the gold standard medication for Parkinson's with the broadest antiparkinsonian effects of any treatment. In the brain, neurons typically convert levodopa to dopamine. Levodopa works by replacing the dopamine lost in Parkinson's. It is combined with carbidopa to prevent nausea and ensure levodopa is not metabolized before it enters the brain.	Carbidopa/Levodopa is the most potent and effective medication for Parkinson's. Parcopa is helpful for people who report daily fluctuations when levodopa wears off. People with Parkinson's should be aware of which preparation they are taking, as there are many different pill sizes, colors, dose strengths and manufacturers. The decision about when to begin using carbidopa/levodopa is different for every person. Because of debate over a possible toxic effect, some people have been reluctant to begin medication; however, studies have shown no evidence of toxicity. Most neurologists agree that delaying treatment may lower quality of life and may put a person at risk for falling.	Early in the Parkinson's course, side effects include low blood pressure, nausea, dry mouth and dizziness. As PD advances, motor side effects such as dystonia and dyskinesia may develop. Confusion and hallucinations are side effects in advanced PD, but less prevalent than hallucinations caused by dopamine agonists. For Stalevo, side effects may include diarrhea, dyskinesia, abdominal pain and harmless discoloration of urine, saliva and/or sweat. The FDA is investigating Stalevo and a possible increased risk of prostate cancer. No conclusions have been made.
Dopamine Agonists Apomorphine (Apokyn®) Bromocriptine (Parlodel®) Pramipexole (Mirapex®) Pramipexole dihydrochloride extended-release (Mirapex ER®) Ropinirole (Requip®) Ropinirole extended-release tablets (Requip® XL™) Rotigotine transdermal system (Neupro®)	Dopamine agonists are drugs that stimulate the parts of the human brain that are influenced by dopamine. In effect, the brain is tricked into thinking it is receiving the dopamine it needs.	In general, this class of medications is not as effective in relieving symptoms of Parkinson's as carbidopa/levodopa. The exception is apomorphine, an injectable dopamine agonist that works rapidly, lasts only 30 minutes or so, and may provoke dyskinesias. Doctors often prescribe agonists as an initial therapy in individuals with Parkinson's, or as a complement to levodopa in people who develop symptom fluctuations. Dopamine agonists should be started in low doses, with a gradual increase in dosage to prevent side effects. Apomorphine requires training in its administration, and is used as a "rescue" therapy for people who experience sudden spells of wearing-off immobility. The rotigotine patch can be advantageous for individuals seeking a long acting medication, as well as those who are undergoing surgery, and cannot swallow.	Mild, common side effects include nausea and lightheadedness due to low blood pressure. More serious side effects can include hallucinations, sedation (including sudden sleepiness, called sleep attacks) and in some people impulse control disorders (impulsive shopping, gambling, hypersexuality and binge eating). Dopamine agonists may also cause dyskinesias, but are less likely than levodopa/carbidopa to do so. Apomorphine may cause severe nausea, and so people using this agent must take an anti-nausea agent. Some clinicians believe that people with PD can develop a withdrawal syndrome when dopamine agonists are stopped, so a gradual decrease in dosage may be advised.
COMT Inhibitors Entacapone (Comtan®) Tolcapone (Tasmar®)	COMT inhibitors are the newest class of PD medications. These agents have no direct effect on PD symptoms, but instead are used to prolong the effect of levodopa by blocking its metabolism.	COMT inhibitors are used primarily to help with wearing-off, a circumstance in which the effect of levodopa becomes short-lived. Entacapone, in addition to being a COMT inhibitor, is also one of the main ingredients in Stalevo, listed under the first class of medications above.	Side effects include abdominal pain, back pain, constipation, nausea, diarrhea and blood in urine. People who take Tasmar must have regular liver function blood tests. In addition to enhancing the positive effects of levodopa, COMT inhibitors may intensify levodopa side effects including hallucinations and dyskinesia.
MAO-B Inhibitors Rasagiline (Azilect®) Selegiline or deprenyl (Eldepryl®) Selegiline HCl orally disintegrating tablet (Zelapar®)	MAO-B inhibitors block an enzyme in the brain that breaks down levodopa.	These drugs have a modest effect in suppressing the symptoms of Parkinson's. They have been shown to delay the need for levodopa when prescribed in the earliest stage of Parkinson's, and have been approved for use in later stages of PD to boost the effects of levodopa. Both rasagiline and selegiline have been studied for possible neuroprotection — i.e., whether the drugs can slow down PD progression. In the case of rasagiline, an FDA advisory committee has concluded that more studies are required before the medication can be approved for this indication.	Depending upon the medication, possible side effects include agitation, dizziness, nausea, headache, rhinitis, back pain, stomatitis, dyspepsia, postural hypotension and indigestion. MAO-B inhibitors may aggravate dopaminergic side effects including dyskinesia and hallucinations. Insomnia is more common with selegiline.

BIOTIE THERAPIES

24 April 2014

Health Care - Finland

Biotie Therapies Summary

Profit & Loss	2011	2012	2013	2014e	2015e
Sales	1	5	28	13	10
EBITDA	-42	-25	2	-4	-10
EBIT	-42	-25	2	-4	-10
Pre-tax profit	-39	-26	4	-4	-11
Net profit	-32	-26	6	-4	-11

Balance Sheet	2011	2012	2013	2014e	2015e
Total assets	118	114	120	116	116
Shareholder´s equity	73	75	81	77	66
Goodwill	6	5	5	5	5
Interest-bearing debt	23	23	21	20	31

Cash Flow	2011	2012	2013	2014e	2015e
EBITDA	-42	-25	2	-4	-10
Chnage in NWC	-13	-12	-7	0	0
Operating cash flow	-44	-37	-5	-4	-10
Free cash flow	-120	-31	-2	-5	-11

Per Share Data	2011	2012	2013	2014e	2015e
EPS	-0.09	-0.06	0.01	-0.01	-0.02
EPS adj.	-0.09	-0.06	0.01	-0.01	-0.02
Operating cash flow per sha	-0.11	-0.08	-0.01	-0.01	-0.02
Book value per share	0.20	0.18	0.18	0.17	0.14
Dividend per share	0.00	0.00	0.00	0.00	0.00
Dividend payout ratio, %	0.0	0.0	0.0	0.0	0.0
Dividend yield, %	0.00	0.00	0.00	0.00	0.00

Ratios	2011	2012	2013	2014e	2015e
P/E	neg.	neg.	20.2	neg.	neg.
P/B	2.6	2.5	1.6	1.3	1.5
P/Sales	192.5	38.4	4.6	8.0	9.9
P/CF	neg.	neg.	neg.	neg.	neg.
EV/Sales	198.1	40.5	5.0	9.2	12.6
EV/EBITDA	neg.	neg.	71.2	neg.	neg.
EV/EBIT	neg.	neg.	71.2	neg.	neg.

Company Description

Biotie is a specialized drug development company focused on products for neurodegenerative and psychiatric disorders. For the past years, Biotie has operated a strategy built around search, profile and partner. This has delivered Selincro (nalmefene) for alcohol dependence, which received European marketing authorization in February 2013 and is currently being rolled out across Europe by partner Lundbeck, and tozadenant, a novel A2a antagonist which is transitioning into Phase 3 development for Parkinson's disease and for which Biotie holds exclusive, global rights. Biotie is actively developing its pipeline assets, including SYN120, a unique potent 5-HT6/5-HT2a dual antagonist for which a Phase 2 study in Alzheimer's diseases is expected to commence recruitment by the end of 2014; nepicastat for treatment cocaine dependency (in Phase 2) and BTT-1023 (Phase 2-ready asset).

Company Miscellaneous

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Major Shareholders

	Capital		Capital
Invesco	17 %	Lundbeck	4 %
UCB Pharma	9 %	Abingworth	4 %
Versant	8 %	Novo A/S	3 %

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Recommendation	Upside potential*
Buy	> 15 %
Accumulate	5 - 15 %
Reduce	-5 - 5 %
Sell	< -5 %

* Potential regarding to 12 month target price

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