1 March 2010

Biotie Therapies Corp

Year End	Revenue (€m)	PBT* (€m)	EPS* (c)	DPS (c)	P/E (x)	Yield (%)
12/08	5.1	(5.6)	(5.6)	0.0	N/A	N/A
12/09	5.6	(12.5)	(7.3)	0.0	N/A	N/A
12/10e	3.2	(13.1)	(8.2)	0.0	N/A	N/A
12/11e	1.4	(9.2)	(5.7)	0.0	N/A	N/A

Note: *PBT and EPS are normalised, excluding goodwill amortisation and exceptional items

Investment summary: Binary events ahead

2010 should be an interesting year for Biotie. Recent positive Phase I rheumatoid arthritis data from VAP-1 antibody BTT-1023, coupled with results of an ongoing study in psoriasis, provide the trigger for the exercise of an option-to-license held by Roche during H110. This could be a means for Biotie to capture significant economic value. Later in the year, results from dose ranging Phase I trials of ELB353 (H110) could also stimulate partnering interest, and read out of the pivotal programme of nalmefene could ensure that Biotie starts 2011 in a stronger financial position.

BTT-1023: Exercise of Roche option is key inflection point

The Phase I data package (including psoriasis) presents a pre-agreed trigger point when Roche can exercise its option over a pre-negotiated licensing deal for the antibody. Another opportunity occurs on completion of Phase II.

Nalmefene: Pivotal data by end-2010

Under the licensing arrangement with Lundbeck, Biotie could receive up to €72m in further milestones: we assume next milestones will be on filing and approval. Positive Phase III data should lead to an MAA filing in H211, with potential launch in 2012.

Financials: Cash of c €20m, funded to key triggers

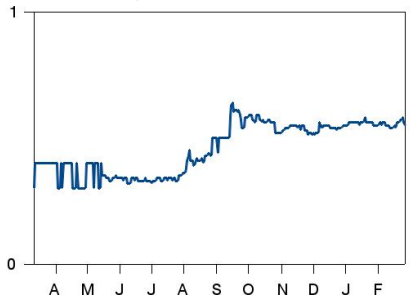
With €19.7m of cash at end-2009, Biotie is funded into 2011 in the absence of new milestones. Potential milestone payments are due from Lundbeck on nalmefene filing and from Roche if the BTT-1023 option is exercised. A Yorkville SEDA arrangement allows Biotie to raise up to €20m of additional equity in *ad hoc* share issues.

Valuation: Risk-adjusted NPV of €150m, EV of €67m

Our rNPV of Biotie's four key R&D programmes continues to indicate a value of €150m. This figure would rise with further positive clinical data. The rNPV compares with a current EV of €67m (not taking into account the €25m Tekes liability as this is only repayable in the event of sustainable profitability).

Price	€0.55
Market Cap	€87m

Share price graph



Share details

Code	BTH1V
Listing	OMX
Sector	Pharmaceuticals & Biotechnology
Shares in issue	158.7m

Price

52-week	High	Low
	€0.67	€0.27

Balance sheet as at 31 December 2009

Debt/equity (%)	N/A
NAV per share (c)	(4.8)
Net cash (€m)	19.7*

** Excluding €25m of capital loans liabilities to Tekes.*

Business

Biotie Therapies is a Finnish/German biotech company with a focus on CNS and inflammatory disease. Its lead project, nalmefene, for the treatment of alcohol dependency, is partnered with Lundbeck.

Valuation

	2009	2010e	2011e
P/E relative	N/A	N/A	N/A
P/CF	N/A	N/A	N/A
EV/Sales	15.3	33.0	84.3
ROE	N/A	N/A	N/A

Revenues by geography

UK	Europe	US	Other
0%	66%	34%	0%

Analysts

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Company description: European CNS specialist

Biotie Therapies is a European biotechnology firm with a strong central nervous system (CNS) and inflammatory disease focus. It has 82 employees and operates from two locations: Turku, Finland and Dresden, Germany. Biotie was founded in Finland in 1992 and merged with two other domestic companies, Contral Pharma and Carbion, in 2002 and subsequently with the German arm of elbion NV in 2008. Elbion was formed as a management buyout of Degussa's pharmaceutical business unit in 2002 and merged with the Belgian firm 4AZA Biosciences in 2006. Biotie listed on the Helsinki stock exchange in 2000 (now NASDAQ-OMX). The company has seen cumulative investment (equity and debt) of €103m (excluding elbion NV) to date.

Valuation

We continue to indicate a valuation of €150m based on a risk-adjusted net present value (rNPV) of the four key programmes in the R&D portfolio. This compares with Biotie's EV of €67m, not taking into account the €25m long-term financial liability due to Tekes, which is repayable only if Biotie becomes sustainably profitable (which would obviously require successful commercialisation).

Sensitivities

Biotie's cash (€19.7m at the year end) should be sufficient to reach beyond the completion of nalmefene's Phase III trial programme at the end of 2010 to the point where regulatory/approval milestones would presumably fall due from Lundbeck. If it exercises its option on BTT-1023 in 2010, further milestones would presumably be payable by Roche. Our valuation is, in our view, conservative, excluding several early-stage programmes and taking a cautious position on the potential market for nalmefene, reflecting in part the fact that the product is not expected to be commercialised in the US (for IP-related reasons).

Financials: Bottom line impacted by exceptional

Revenues were €5.6m (€7.2m including €1.8m of grant income) in 2009, consisting principally of recognition of previously received milestone payments. Biotie recorded a net loss of €16.1m (including a €5.4m non-cash impairment charge). Biotie has long-term liabilities of €26m (mostly capital loans from Tekes, the Finnish Funding Agency for Technology and Innovation, which are repayable only on successful commercialisation on the programme to which they relate), which with cash of €19.7m means that net debt stands at €6m. Biotie is funded to the end of 2011, when milestones are presumed to fall due from Lundbeck on the nalmefene programme.

Investment summary: Unlocking value in VAP-1

The longer-term investment case for Biotie Therapies centres on nalmefene, an oral on-demand therapy for moderating heavy drinking, which is in Phase III studies funded by partner Lundbeck, which effectively has worldwide rights. Biotie's c€20m cash at end-2009 should be sufficient to last to the availability of Phase III data on nalmefene in late 2010/2011, with milestones are presumed payable on regulatory filings and approvals. However, Biotie's next likely catalyst is the exercise of the Roche option for global ex-Asia rights to VAP-1 antibody BTT-1023, which may occur during H110. The terms of this licensing deal are undisclosed, but are described as 'company changing'.

BTT-1023 and Biotie's broader R&D pipeline mitigate, to some extent, the single product risk in nalmefene. The company has four key R&D programmes: nalmefene (now prominently featured in Lundbeck's investor presentations and due to report pivotal data by year end), ELB-353 (seeking a partner once the ongoing Phase I study reads out in H110), BTT-1023 (Roche may exercise its option to global ex-Asia rights in H110), and the PDE10 inhibitor programme (which may enter the clinic this year).

Biotie's R&D programmes and partners are presented in Exhibit 1.

Exhibit 1: Biotie Therapies R&D portfolio

Product	Indication/stage	Partners/ financial terms/notes
Nalmefene	Alcohol dependence (Phase III)/ pathological gambling/ smoking cessation	Partnered with **Lundbeck** worldwide (excluding South Korea), in a deal providing up to €84m in upfront and milestone payments (of which €12m has been received to date) and tiered double-digit royalties. Licensed to **Whanin Pharmaceutical** (South Korea). Undisclosed small royalty payable to **Teva** for exclusive right to IP on nalmefene use in impulse control disorders and access to US regulatory package. Lundbeck is conducting two identical placebo-controlled Phase III studies, each in 600 pts (ESSENCE1 and ESSENCE2) using 20mg nalmefene on demand (primary efficacy endpoints are change in baseline in the monthly number of heavy drinking days and total alcohol consumption over 24 weeks, results due Feb 2011). It is also conducting a 677-pt, 52-week Phase III study (SENSE) to focus on safety and tolerability (fully recruited, results: Nov 2010). Possible EU filing in H211, launch in 2012/13.
ELB-353	COPD/asthma/ psoriasis (Phase II-ready)	Orally available phosphodiesterase-4 (PDE4) inhibitor (differentiated by improved side-effects vs other PDE4 inhibitors, particularly a lack of GI/CNS side-effects). Repeat dose PK studies underway in 48 healthy volunteers to establish safety profile and dose range for therapeutic studies (results: H110). Phase II studies in psoriasis are possible, but most likely to be partnered for further development in chronic obstructive pulmonary disease.
BTT-1023 Fully human VAP-1 antibody	Rheumatoid arthritis/psoriasis (Phase I)/ ulcerative colitis (preclinical)	Agreements with **Roche** (option for worldwide licensing deal, excluding Asia/Australia) and **Seikagaku** (licensing deal for Japan, Taiwan, Singapore, New Zealand and Australia). Roche paid a total of €8m to acquire and maintain the exclusive option, and has first opt-in opportunity at end of Phase I (mid-2010), or may pay an option extension fee for another opt in opportunity, at end of Phase II. The agreement with Seikagaku included a signing fee of $2.5m and $14.2m of milestones. Repeat-dose Phase I studies in 24 RA patients showed PK consistent with chronic use and some evidence of efficacy at higher doses. Results of a similar ascending multiple dose study in 41 psoriasis patients are due in Q210. Fully human MAb for vascular adhesion protein-1 (VAP-1) generated by Medarex Humab technology.
VAP-1 SSAO inhibitor	Inflammatory disease (preclinical)	Option agreements with **Roche** (which may pay up to €5m to maintain its exclusive option for global ex-Asia rights) and **Seikagaku** (if exercised, Biotie will receive up to $16.7m in milestones plus royalties on sales for Asian rights). VAP-1 semicarbazide-sensitive amine oxidase (SSAO) enzyme contributes to production of molecules that exacerbate inflammation.
PDE10 inhibitor	Schizophrenia/ bipolar disorder (preclinical)	Partnered with **Pfizer** in deal valued at up to $110m in signing fee, milestones, plus research funding ($14m received to date) and double-digit royalties on sales. IND possible in early 2010. Expected to offer improved side-effects vs atypicals, eg lack of weight gain.
A2ß1 integrin inhibitor	Thrombosis (preclinical)/ cancer	Positive results in several animal models of inflammation demonstrate significant potential in inflammatory diseases. Also thought to be a mediator in the formation of metastases into bone (eg from prostate cancer). Collaborations with the University of Turku, Åbo Akademi University and the University of Jyväskylä.
PDE 2/PDE 7	Research	Internal research programmes.

Source: Edison Investment Research

VAP-1 programmes: potential option exercise in H1

Biotie has two approaches targeting vascular adhesion protein-1 (VAP-1): a fully human VAP-1 monoclonal antibody, BTT-1023[1], which is a first-in-class selective adhesion molecule inhibitor for inflammation, and a small molecule VAP-1 SSAO (semicarbazide-sensitive amine oxidase) inhibitor.

VAP-1 is an adhesion molecule expressed on endothelial cells lining blood vessels which mediates entry of white blood cells into sites of inflammation. A key feature of VAP-1 is its specificity: it is expressed in a functional form only at the site of inflammation. Both VAP-1 and VAP-1 SSAO (semicarbazide-sensitive amine oxidase) contribute to production of molecules that exacerbate inflammation; inhibiting VAP-1 or VAP-1 SSAO reduces inflammation by reducing leukocyte migration to inflamed tissues, a common feature in many autoimmune diseases (eg rheumatoid arthritis, ulcerative colitis and psoriasis).

Biotie has partnered its antibody and small-molecule inhibitor programmes separately on a territorial basis with Roche (worldwide, excluding Asia) and Seikagaku (Asia). Roche has an option on both programmes, while Seikagaku has a licence agreement for BTT-1023 and an option on VAP-1 SSAO. Of the two programmes, BTT-1023 is further in the clinic: in January, a positive outcome of its 24-pt Phase I trial in rheumatoid arthritis was reported. These data (possibly including the results from a Phase I study in psoriasis, due in Q210), provide a first pre-agreed trigger point for the option-to-license held by Roche. Biotie indicates that Roche will be required to decide whether to exercise its option in H1 this year (if not exercised, there is a second opportunity after Phase II).

The potential licensing deal for BTT-1023 with Roche is an important event from an investment perspective. The financial terms of the potential deal with Roche have not been disclosed but are described as being of a 'company changing' magnitude, which we would suggest indicates a headline value (upfront and milestones) in excess of $250m. It is also important to appreciate that while Biotie is approaching the first of the two trigger points for option exercise by Roche, we understand that Biotie can decline to accept the first option and thereby attempt to capture greater value by funding Phase II studies.

Nalmefene: central to Biotie's longer-term investment case

Nalmefene is an opioid receptor antagonist designed to prevent the neurochemical reward and reinforcement signals associated with craving in impulse control disorders. It is structurally similar to naltrexone, which is also used for treating alcohol dependency, but has important pharmacological advantages, including a lack of dose-dependent liver toxicity, greater oral bioavailability, longer duration of antagonist action, and more competitive binding with opioid receptor subtypes that are thought to reinforce drinking. Nalmefene has also been investigated in other impulse control disorders such as pathological gambling and smoking.

The Danish CNS-focused pharmaceutical group, Lundbeck has global nalmefene rights (excluding Turkey and South Korea, where it is licensed to local companies). It signed an initial licensing deal

in 2006, and more recently obtained North American rights after these were recovered from former licensee, Somaxon Pharmaceuticals. Given that nalmefene is available in an IV formulation in the US, effective commercial exclusivity for treatment of alcohol dependency is limited.

Controlling heavy drinking rather than maintaining abstinence

Biotie is seeking to position nalmefene as an aid to controlling/moderating heavy drinking, rather than to maintain abstinence, which is the focus of existing alcohol dependency treatments. This strategy has a number of advantages, especially as it is intended that nalfemene would ultimately be prescribed predominantly by primary care physicians, thus making it more widely available. Advantages include the fact that patients would not be labelled alcoholics – they would take the drug only as needed, and therefore would not have to enrol on psychosocial counselling programmes or have a minimum period of abstinence prior to treatment, as is the case for other therapies and is a major limitation for logistical reasons.

Biotie's approach is controversial since abstinence has historically been promoted as the prime objective in treating alcohol dependence; however, this is a very challenging treatment goal. A strategy of moderating intake may be a more feasible treatment goal for many alcohol abusers, particularly as alcohol dependence is now also increasingly viewed as a chronic recurring disorder where relapses are almost inevitable.

Harm reduction strategy

The key benefit of a control/moderation strategy is harm reduction: patients who are able to moderate excessive alcohol intake (and drink less in total) should be able to reduce morbidity and mortality associated with alcohol abuse. In addition to well known alcohol-linked conditions such as liver cirrhosis, heavy drinking has also been linked to an elevated risk of developing liver, colorectal and pancreatic cancers. Studies have also shown that even a moderate reduction in alcohol intake can significantly reduce liver damage: and the societal burden from risks (eg violence, accidents, etc) arising from excessive drinking is large. Datamonitor estimates that in the UK alone, there are 150,000 hospital admissions and 20,000 premature deaths thought to be directly due to alcohol and 1.2m alcohol related violent incidents, with the annual cost of alcohol abuse to the NHS estimated at £1.4-1.7bn/year. It is also estimated that there are more than 30m alcohol abusers in the US, the EU and Japan, making this a potentially large, if undeveloped, market opportunity.

IP issues: Data protection only

Nalmefene is available in the US as an injectable product, Revex (sold by Ivax/Teva) indicated for the reversal of opioid effects (eg in the case of overdose). Biotie acquired exclusive rights to IP on nalmefene use in impulse control disorders and access to the US regulatory package from Ivax, in exchange for a small royalty on sales. Nalmefene's basic composition-of-matter patent has expired, hence IP protection on the oral formulation will largely rely on 10-year regulatory market exclusivity from first launch in the EU (and seven years in the US). In the US, the period of exclusivity would be reduced and any product would have to rely on method-of-use patents (hence it was being profiled by Somaxon for pathological gambling and smoking cessation).

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[1] Biotie has earlier clinical validation of the anti-VAP strategy from studies with murine (vepalimomab) and chimaeric (vapaliximab, BTT-1002) versions of BTT-1023. However, the pharmacokinetic profiles of the early

Clinical trials

Nalmefene has been studied in various clinical trials. Biotie conducted two positive Phase III studies in the UK and Finland in alcoholism and alcohol dependence (although the smaller UK study did not reach statistical significance due to a high rate of drop out); and Somaxon conducted three studies, two in pathological gambling – with mixed clinical evidence – and one in smoking cessation. An independent academic study of naltrexone and nalmefene in pathological gambling identified a positive family history of alcoholism as the clinical variable most strongly associated with a positive response to an opiate antagonist (p=0.006)[2].

Key clinical trial results are summarised in Exhibit 2.

Exhibit 2: Clinical studies of nalmefene

Note: HDD = heavy drinking days (males ≥5 standard drinks, females ≥4 standard drinks); PG-YBOCS = Yale Brown Obsessive Compulsive Scale modified for Pathological Gambling; CBT = Cognitive Behavioural Therapy

Indication	study	Results
Alcohol dependence	Phase III (CPH-101-0801) Finland	403-pt study of nalmefene (10-40mg) or placebo taken PRN 1-2 hours before expected alcohol use. 60% of nalmefene arm and 68% of placebo arm completed initial 28 weeks. On average, nalmefene arm took a pill on 35% of days, and the placebo arm on 44% of days. Over the initial 28 weeks, risk of HDDs was 32% lower in the nalmefene arm vs placebo. Nalmefene-treated patients experienced a c 40% reduction in HDD per month vs baseline (15.5/month), which was sustained over seven months vs 20-30% reduction vs (16.2 HDD/month) for placebo (p=0.0065). After 28 weeks, good responders on nalmefene were randomised to continue on nalmefene or placebo for an additional 24 weeks. Among good responders, those who continued nalmefene had a lower mean proportion of HDD than those who switched to placebo (18% vs 30%). Post hoc analysis showed cumulative HDD were around 30% lower on nalmefene vs placebo over 200 days[3].
Alcohol dependence	Phase III (CPH-101-0701) UK	167-pt study showed 50-60% reduction in HDD/month vs baseline, vs 30-40% reduction for placebo over month two to seven (effect size was lower in month one). High drop-out rate compromised statistical power: significance missed (p=0.088, group/time). Several secondary endpoints met.
Alcohol dependence	Academic study	105-pt abstinent for a mean of two weeks prior to randomisation. Pts assigned to oral nalmefene (n=70) at a 20 mg/day (10mg twice daily) or 80 mg/day (40mg twice daily) dose, or placebo (n=35) for 12 weeks. CBT provided weekly during treatment. Reported drinking or abstinence confirmed by determination of breath alcohol concentration and by collateral informant reports. Significantly fewer pts treated with nalmefene vs pts on placebo relapsed to heavy drinking through 12 weeks of treatment (p<0.02), with a significant treatment effect at the first weekly study visit (p<0.02). The odds ratio of relapsing to heavy drinking was 2.4 times greater with placebo vs nalmefene (95% CI 1.05-5.59). Pts treated with nalmefene also had fewer subsequent relapses (p<0.03) than pts given placebo. Outcomes did not differ between the 20 and 80mg dose nalmefene group[4].
Pathological gambling	Phase II/III	Somaxon-sponsored 233-pt study of nalmefene (20mg and 40mg) failed to demonstrate an effect on PG-YBOCS after 12 weeks of treatment; neither dose achieved significance on secondary endpoints.
Pathological gambling	Phase II	207-pt, 16-week dose-ranging trial of nalmefene (25mg/day, 50mg/day, or 100mg/day) vs placebo. Primary outcome measure: PG-YBOCS score. Results: pts on 25mg/day and 50mg/day nalmefene showed significant improvement vs placebo. 59.2% of pts on 25mg/day were considered responders at last evaluation, compared to 34.0% on placebo, with few adverse events. Higher doses (50mg/day and 100mg/day) resulted in intolerable side-effects (ie nausea, dizziness and insomnia)[5].
Smoking cessation	Pilot Phase II	Somaxon-sponsored trial in 76 smokers showed numerically higher abstinence rates relative to placebo in the 40mg group, but not in 80mg group.

Source: Edison Investment Research

Lundbeck-sponsored Phase III studies underway

Three Phase III studies in a total of 1,800 patients are underway and should read out in H111, supporting a European marketing authorisation application for nalmefene later that year, with potential launch in 2012. Two of the trials (ESENSE1 and ESENSE2) are identical 600 patient

products were not consistent with the requirements for treating chronic conditions.

2 Grant *et al,* Psychopharmacology (Berl). 2008 Nov; 2000(4):521-7.

3 Karhuvaara *et al*, Alcohol Clin Exp Res. 2007 Jul; 31(7):1179-87.

4 Mason *et al*, Arch Gen Psychiatry. 1999 Aug; 56(8):719-24.

5 Grant *et al* Am J Psychiatry 163: 303-312, February 2006.

placebo-controlled studies using a 20mg dose, evaluating rates of excessive alcohol consumption (ie heavy drinking days - HDD) and overall alcohol intake per month over 24 weeks, as well as various functional and medical parameters. The third SENSE study is a 52-week, 668 patient trial focused on safety and tolerability. In our view, it will be important that the studies show a clinically meaningful reduction in overall alcohol intake in addition to a reduction in the number of HDD.

Approved products require abstinence, detox and psycho-social support

All four products approved for treatment of alcoholism (Exhibit 3) require patients to be abstinent (to have undergone detoxification) and be supported by a psycho-social programme. Nalmefene is the first product to have shown efficacy in controlled studies without concurrent psycho-social intervention. The c 30% reduction in the HDDs seen with nalmefene is also greater than that seen in published studies of Vivitrol of c 25% for high dose and 18% for lower dose[6].

Exhibit 3: Treatments for alcohol dependence

Drug	Company	Development stage/notes
Campral (acamprosate)	Forest Labs (US)/Merck KGaA (RoW)	Indicated for maintenance of abstinence from alcohol in alcohol dependent pts who are abstinent at treatment initiation. Three positive clinical trials (from 90 days to 360 days) in a total of 998 alcohol-dependent pts who had undergone inpatient detoxification and were abstinent at baseline. Negative study in pts who had not undergone detoxification and/or were not abstinent at baseline.
Vivitrol (naltrexone extended release depot)	Alkermes (US)/J&J (Russia/CIS)	Marketed in US and Russia. Indicated for treatment of alcohol dependence in patients who are able to abstain from alcohol prior to treatment initiation. Six-month Phase III showed reduction in HDDs against background of psycho-social support. Greater effect seen in subset of patients who abstained completely from drinking in the week prior to receiving medication (reductions in the number of drinking days (97% difference; p=0.02) and HDDs (92% difference, p<0.05). Once monthly intramuscular injection. Recent FDA warning on skin reactions.
Naltrexone (oral)	Various – generic	Widely approved. Systematic review of 27 clinical trials shows short-term treatment decreases the chance of alcohol relapses by 36% and chance of returning to drinking by 13%[7].
Disulfiram (Antabuse)	Barr Laboratories	Approved for >50 years. Aversive agent that causes unpleasant reactions (flushing, headache, nausea, difficulty breathing, chest pain, collapse) if alcohol is taken subsequently.

Source: Edison Investment Research

Leading product in clinical trials for alcohol dependence

While nalmefene is the leading clinical-stage therapy for alcohol dependency, there are competing development programmes by Lilly and Schering-Plough/Merck & Co. However, in the context of an undeveloped market, a number of potential new entrants advocating pharmacotherapy is an advantage.

Other development programmes can be found in Exhibit 4.

[6] Garbutt *et al* JAMA, 2005; 293;1617-25.

[7] Srisurapanont *et al.* Cochrane Database Syst Rev. 2005 Jan 25; (1):CD001867.

Exhibit 4: Competitive developments for treatment of alcohol disorders

Note: NIAAA= National Institute on Alcohol Abuse and Alcoholism (part of US National Institutes of Health).

Drug	Company	Development stage/notes
Org 25935	Merck & Co	300-pt, 12 week Phase II study in relapse prevention in subjects with alcohol dependence (results: Nov 2010). Drug taken in the morning and in the evening. Glycine reuptake inhibitor.
LY686017	Lilly	190-pt 12-week Phase II for alcohol dependence complete (once daily dosing): data not yet disclosed. 50-pt Phase II study in recently detoxified alcoholic pts (1:1 randomisation) showed suppression of spontaneous alcohol cravings, improved overall wellbeing, reduced challenge-induced craving and attenuated concomitant cortisol responses. NK-1 antagonist.
LY2196044	Lilly	360-pt 16-week Phase II study for alcohol dependence (results: March 2010). Administered four times daily, titrated over first two weeks. Possibly opioid receptor antagonist project also known as OpRA II.
MK-0594	Merck & Co	162-pt 12-week Phase II (results: Oct 2014). Five arm study of two daily doses (1mg and 5mg) and one weekly dose (1/mg), after initial loading dose. Previously studied in overactive bladder. Study protocol changed from 1,500-pt study Feb 2010.
ALKS 33	Alkermes	440-pt 12-week Phase II trial in alcohol dependence (results: Oct 2011). Oral opioid modulator.
ALKS 29	Alkermes	Oral combination of extended-release baclofen and ALKS 33. Components currently under separate evaluation. Favourable PK profile for both constituents in two separate16-pt studies.
Various single agents	NIAAA/academic groups	Multiple Phase II trials including zonisamide, gabapentin, levetiracetam, quetiapine, mecylamine, topiramate, prazosin, varenicline and olanzepine.
Various combination therapies	NIAAA/academic groups	Multiple Phase II trials of drug combinations including ondansetron + naltrexone (320-pt, results: Jan 2012), aripriprazole + topiramate (216-pt, results: Jul 2012), ondansetron + topiramate, disulfam + lorazepine, naltrexone + aripiprazole, naltrexone + baclofen, disulfam + lorazepam.
Naltrexone Depot	Elbion NV	In-licensed from DrugAbuse Sciences; excluded from Biotie's acquision of elbion.
DOV 102677	Dov Pharma	Phase I. Repeat dose studies in volunteers previously planned for 2009, funding permitting. Euthymics Bioscience signed non-binding letter of intent to merge and acquire Dov (Feb 2010).

Source: Edison Investment Research

ELB-353: partner sought

Biotie is seeking to partner ELB-353, a PDE-4 inhibitor in development for COPD and psoriasis, once additional PK and dosing studies read out in H110. These studies are designed to identify the maximum tolerated dose, and perhaps demonstrate a wider therapeutic window than competing PDE-4 compounds.

PDE-4 is an attractive mechanism for asthma/COPD treatment, but has historically been beset by clinical failures due to the narrow therapeutic window seen in some developmental programmes, and the potential for gastrointestinal side effects. Nycomed's Daxas (roflumilast), PDUFA date May 20, is likely to be the first-in-class PDE-4 inhibitor in COPD.

Exhibit 5 summarises the competition.

Exhibit 5: PDE4 inhibitors competitive landscape

Drug	Company	Development stage/notes
Daxas (roflumilast)	Nycomed/ Forest (US)/ Mitsubishi Tanabe (Japan)	Registration: filed with EMEA (May 2009) and FDA (June 2009). Four positive Phase III studies in 4,500-pts: two pivotal 12-month trial (HERMES and AURA) vs placebo, and two six-month trials (EOS and HELIOS) in combination with salmeterol or tiotropium. All trials showed sig. reduction in exacerbations (between 15%-37%) and sig. lung function improvement. Oral once daily.
OX914	Orexo	Planned development in asthma/COPD following partnership. 36-pt Phase IIa study in pollen-allergic pts showed no effect vs placebo on patient symptom scores after allergen challenge. CAPSICS asthma study (by previous owner Inflazyme [as IPL-455903]) showed no effect. Oral.
Apremilast/ CC-10004	Celgene	260-pt Phase II in plaque psoriasis showed 24.4% of apremilast arm achieved >75% reduction in baseline PASI score after 84 days (p=0.023) vs 10.3% of placebo (similar stat. sig. for >50% and >90% reduction in baseline PASI). 348-pt Phase IIb moderate/severe psoriasis (results: 2010) and exploratory trials (rheumatic, dermatologic and inflammatory disease) ongoing. Oral.
Oglemilast	Glenmark/ Forest/Teijin	Topline results from 428-pt 12-week Phase IIb in COPD did not show stat. sig. increase in FEV_1 from baseline vs placebo. 282-pt Phase IIb study in asthma ongoing (results: Q110). Oral.
Tetomilast	Otsuka	180-pt Phase II/III in Crohn's disease (results: June 2012); 720-pt Phase II in COPD (results: May 2013), 100-pt Phase II in COPD associated with emphysema (results: July 2012). Oral.
ASP9831	Astellas	105-pt 12-week Phase II study for non-alcoholic steatohepatitis (results: June 2010). Oral.
AN2728	Anacor	140-pt 12-week Phase II study for plaque psoriasis (results: Nov 2010). Topical.
MN166 (ibudilast)	MediciNova	Two year Phase II in multiple sclerosis demonstrated potential disease-modifying effect. No further development in absence of partner. Sold in Japan by Kyorin for asthma. Oral.
AV-411 (ibudilast)	Avigen	30-patient Phase II sponsored by NIDA in opioid withdrawal. Possible future development for chronic neuropathic pain, opioid and methamphetamine addiction. Oral.
ONO 6126	Ono/Santen	Phase II conducted in COPD/asthma. Licensee developing in ophthalmic indications. Oral.

Source: Edison Investment Research

Valuation

We continue to indicate a valuation of €150m based on a risk-adjusted net present value (rNPV) of the four key programmes in the R&D portfolio, using a 12.5% cost of capital (Exhibit 6). This uses industry standard development probabilities, our estimates of market size and potential, and economics of possible and actual partnering deals, where known. This valuation increases as products move successfully through development and justify higher probabilities of success.

Exhibit 6: Biotie's core business rNPV model

Product(s)	Status	Probability of success	Est launch year	Est peak market share	Current market value	Est maximum royalty	Est peak sales
Nalmefene	Phase III	65%	2012	50%	$750m	15%	$567m
ELB353	Phase II	35%	2014	3%	$15,000m	18%	$681m
BTT-1023	Phase I	15%	2014	2%	$27,000m	15%	$540m
VAP-SSAO	Preclinical	5%	2015	2%	$27,000m	15%	$469m

Source: Edison Investment Research

We compare this €150m valuation with Biotie's current EV of €67m. Note that the calculation of EV does not consider the €25m long-term financial liability due to Tekes, since the majority of this is repayable only if Biotie becomes sustainably profitable.

Sensitivities

The key sensitivities for Biotie are similar to any biotech company, and include the unpredictable nature of clinical trials and the reliance on a small number of development programmes and partners. Biotie's cash position is relatively strong and should be sufficient to reach beyond the completion of the nalmefene Phase III trial programme in 2010 to the point where milestones are presumed to fall due. Our valuation is, in our view, conservative, excluding several early-stage programmes and taking a cautious view on the potential market for nalmefene, reflecting in part the fact that US commercialisation (for IP-related reasons) is unlikely.

Financials

Biotie reported 2009 revenue of €5.6m (€7.2m including €1.8m of grant income), largely from the deferred recognition of previously received payments from partners. R&D costs of €21.1m in 2009 included a €5.4m non-cash impairment charge related to the termination of various programmes. We expect R&D spend to be around €13m in 2010, although this is difficult to predict at this point and is highly dependent on whether Roche exercises its option to license BTT-1023. Biotie declined to provide 2010 financial guidance, as its performance will be contingent upon the outcome of a number of binary events during the year. Our model does not, at this point, assume the exercise of Roche's option to BTT-1023.

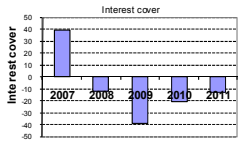
Biotie ended 2009 with cash and equivalents of €19.7m; however, as the company has €25.6m of long-term financial liabilities (mostly loans from Tekes, the Finnish Funding Agency for Technology and Innovation), our model shows net debt of €6m. It is important to note that these liabilities are largely repayable only in the event Biotie becomes sustainably profitable. Our model suggests Biotie is funded to late 2011 in the absence of any potential milestones. Biotie also has a SEDA (Standby Equity Distribution Agreement) financing facility with Yorkville Advisors, a US investment company that specialises in such products. Under this facility, Biotie, at its discretion, can raise up to €20m in total, over the 36 months to October 2012, through share issue in small tranches at a fixed, narrow (c 5-10%) discount to the prevailing VWAP.

Our financial model is shown in Exhibit 7.

Exhibit 7: Financial model

Year end 31 December	€'000s	2007	2008	2009	2010e	2011e
Accounting basis		IFRS	IFRS	IFRS	IFRS	IFRS
PROFIT & LOSS						
Revenue		**7,895**	**5,127**	**5,628**	**3,203**	**1,375**
Cost of Sales		0	0	0	0	0
Gross Profit		7,895	5,127	5,628	3,203	1,375
EBITDA		**(1,581)**	**(4,874)**	**(12,231)**	**(12,247)**	**(8,233)**
Operating Profit (before GW and except.)		**(1,699)**	**(5,121)**	**(12,231)**	**(12,547)**	**(8,533)**
Goodwill Amortisation		0	0	0	0	0
Exceptionals		0	0	(5,400)	0	0
share option charge		0	0	0	0	0
Operating Profit		**(1,699)**	**(5,121)**	**(17,631)**	**(12,547)**	**(8,533)**
Net Interest		43	(432)	(311)	(600)	(650)
Profit Before Tax (norm)		**(1,656)**	**(5,553)**	**(12,542)**	**(13,147)**	**(9,183)**
Profit Before Tax (FRS 3)		**(1,656)**	**(5,553)**	**(17,942)**	**(13,147)**	**(9,183)**
Tax		0	76	1,859	125	71
Profit After Tax (norm)		(1,656)	(5,477)	(10,683)	(13,022)	(9,111)
Profit After Tax (FRS3)		(1,656)	(5,477)	(16,083)	(13,022)	(9,111)
Average Number of Shares Outstanding (m)		90.0	97.0	145.5	158.8	158.8
EPS - normalised (c)		**(1.8)**	**(5.6)**	**(7.3)**	**(8.2)**	**(5.7)**
EPS - FRS 3 (c)		**(1.8)**	**(5.6)**	**(11.1)**	**(8.2)**	**(5.7)**
BALANCE SHEET						
Fixed Assets		**1,079**	**13,523**	**10,241**	**9,981**	**9,730**
Intangible Assets		747	10,731	7,565	7,565	7,565
Tangible Assets		332	2,792	2,666	2,416	2,165
Investment in associates		0	0	10	0	0
Current Assets		**28,996**	**29,281**	**21,285**	**9,224**	**3,612**
Debtors		753	3,912	1,507	2,000	2,000
Cash		28,243	25,369	19,778	7,224	1,612
Other		0	0	0	0	0
Current Liabilities		**(7,477)**	**(6,363)**	**(6,060)**	**(4,329)**	**(2,953)**
Group borrowings		(1,632)	(2,718)	(3,890)	(2,811)	(2,811)
Provisions		(104)	(144)	(217)	(143)	(142)
Other current liabilities		(5,741)	(3,501)	(1,953)	(1,375)	0
Long Term Liabilities		**(33,715)**	**(31,506)**	**(33,029)**	**(32,563)**	**(37,160)**
Long term borrowings		(23,603)	(24,930)	(25,597)	(25,403)	(30,000)
Provisions		(14)	(121)	(160)	(160)	(160)
Other long term liabilities		(10,098)	(6,455)	(12,440)	(11,825)	(8,375)
Net Assets		**(11,117)**	**4,935**	**(7,563)**	**(17,687)**	**(26,771)**
CASH FLOW						
Operating Cash Flow		**(4,882)**	**(9,763)**	**(11,409)**	**(12,628)**	**(9,608)**
Net Interest		17	37	(58)	(600)	(650)
Tax		0	76	(1,859)	992	98
Capex		(23)	(34)	(165)	(50)	(49)
Acquisitions/disposals		0	1,881	0	0	0
Financing		139	2,938	7,202	0	0
Dividends		0	0	0	0	0
Net Cash Flow		**(4,749)**	**(4,865)**	**(6,289)**	**(12,286)**	**(10,208)**
Opening net debt/(cash)		**(8,229)**	**(4,536)**	**(295)**	**6,036**	**18,322**
HP finance leases initiated		0	0	0	0	0
Other		1,056	624	(42)	0	0
Closing net debt/(cash)		**(4,536)**	**(295)**	**6,036**	**18,322**	**28,530**

Source: Edison Investment Research

Growth	Profitability	Balance sheet strength	Sensitivities evaluation	
N/A	N/A		Litigation/regulatory	●
			Pensions	○
			Currency	◖
			Stock overhang	○
			Interest rates	◖
			Oil/commodity prices	○

Growth metrics	%	Profitability metrics	%	Balance sheet metrics		Company details	
EPS CAGR 07-11e	N/A	ROCE 2010e	N/A	Gearing 10e	N/A	Address:	
EPS CAGR 09-11e	N/A	Avg ROCE 07 to 11e	N/A	Interest cover 10e	N/A	Tykistökatu 6 FI-20520 Turku Finland	
EBITDA CAGR 07-11e	N/A	ROE 2010e	N/A	CA/CL 10e	2.1		
EBITDA CAGR 09-11e	N/A	Gross margin 2010e	N/A	Stock turn 10e	0.0	Phone	+35 82274 8900
Sales CAGR 07-11e	N/A	Operating margin 10e	N/A	Debtor days 10e	227	Fax	+35 82274 8910
Sales CAGR 09-11e	N/A	Gross mgn/Op mgn	N/A	Creditor days 10e	250	www.biotie.com	

Principal shareholders	%
TVM Capital	12.3
Pequot	9.6
Invesco Asset Management	9.1
Finnish Innovation Fund (Sitra)	8.6
Burrill & Co	6.6
Veritas Asset Management	4.2

Forthcoming announcements/catalysts	Date *
AGM	15 April
Q110 results	7 May
Phase II psoriasis results for BTT-1023	Q2
H110 results	6 August
Q310 results	29 October
*Note: * = estimated*	

Management team

CEO: Dr Timo Veromaa (Finnish)

President and CEO since 2005, previously vice-president of R&D (1998-2005). Previous roles include: medical director, Schering Oy, Finland (1996-1998), research and programme manager, Collagen Corp, US (1994-1996).

CFO: Dr Thomas Taapken (German)

CFO of Biotie since 2008. Previously CFO of Elbion (2005-2008). Earlier positions include: partner, life science team of DVC Deutsche Venture Capital, and various roles in research, corporate development and venture capital at Sanofi-Aventis.

Chairman: Juha Jouhki (Finnish)

Director since 2002 and chairman since 2005. Managing director of Biothom Oy. Previsouly at Thominvest Oy (partner 199-2002; MD 2002-2009). Also chairman of Dreadnought Finance Oy, Thomcapital Oy, Procarbon AB, Neomedit Oy, Alimetrics Oy and Ram Partners Oy. Director of Northern Antibiotics Oy.