EDISON

Bionor Pharma

Initiation of coverage

Aiming high in HIV

Pharma & biotech

Bionor Pharma's ambitious aim to develop Vacc-4x as the first functional cure for HIV is supported by previous data and collaborations with leading institutes. A comprehensive 'Kick, Kill and Boost' strategy is in place and recent funding should allow Bionor to take Vacc-4x through the critical steps prior to partnering. Key 'Kill' and 'Boost' data are expected in Q214. We value Bionor at NOK4.0/share, based on prudent Vacc-4x assumptions.

Year end	Revenue (NOKm)	PBT* (NOKm)	EPS* (NOK)	DPS (NOK)	P/E (x)	Yield (%)
12/11	109.5	61.3	0.33	0.0	9.0	N/A
12/12	4.2	(55.2)	(0.29)	0.0	N/A	N/A
12/13e	4.3	(60.3)	(0.29)	0.0	N/A	N/A
12/14e	1.6	(63.3)	(0.29)	0.0	N/A	N/A

Note: *PBT and EPS are normalised, excluding intangible amortisation, exceptional items and share-based payments.

Vacc-4x could be the first functional cure for HIV

Bionor is developing Vacc-4x as a potential functional cure for HIV. Vacc-4x is one of the furthest advanced therapeutic vaccines in development, and has already demonstrated efficacy against HIV. Bionor's 'Kick, Kill and Boost' development strategy encompasses all the elements required to achieve a functional cure for HIV. These include releasing dormant HIV reservoirs (Kick), encouraging HIV destruction via an immune response elicited by Vacc-4x (Kill) and strengthening the immune system to maximise its attack on HIV (Boost).

Previous data support strategy; further data in H114

Previous trials have consistently demonstrated efficacy. Most recently Vacc-4x has demonstrated a significant 64% viral load reduction versus placebo, and a significant 60% reduction compared to levels before antiretroviral treatment (ART) was initiated. Two trials are ongoing: a Vacc-4x reboost trial investigating further viral load reduction, with data expected Q114; and a combination with Revlimid (an immune modulator) as part of a Celgene collaboration, aiming to boost the immune system to enhance the Vacc-4x response, with data expected Q214.

Substantial market for an HIV cure

There are c 1.1m HIV-infected patients in the US, and c 1m in the developed EU. The global ART market was worth c $17bn in 2012. In the US only 25% of HIV patients are virally suppressed, despite 33% receiving ART treatment. Although Vacc-4x is being developed as a functional cure, at this stage we more prudently forecast peak sales of €1.3bn, assuming it becomes an additional HIV treatment. If Vacc-4x is successfully developed as a cure this could offer upside to our forecasts.

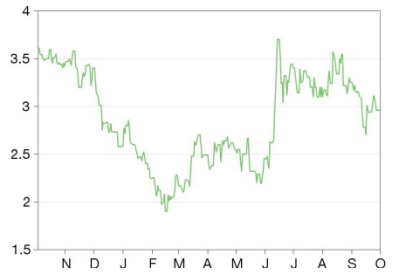
Valuation: Risk-adjusted NPV of NOK868m

We value Bionor at NOK868m or NOK4.0/share based on a risk-adjusted NPV analysis, which includes net cash and Vacc-4x. NOK129m net cash including the NOK54.5m private placement should be sufficient to fund operations to mid-2015.

3 October 2013

Price	**NOK2.97**
Market cap	**NOK671m**
	NOK7.84/€
Net cash (NOKm) as at end-June 2013	74.8
Shares in issue	218.3m
Free float	59.7%
Code	BIONOR
Primary exchange	Oslo
Secondary exchange	N/A

Share price performance



%	1m	3m	12m
Abs	(7.0)	(11.9)	(17.9)
Rel (local)	(6.7)	(16.0)	(22.2)
52-week high/low	NOK3.69		NOK1.9

Business description

Bionor Pharma is a Norwegian biotechnology company focused on developing peptide vaccines for infectious diseases. The lead product, Vacc-4x, is currently in Phase II development as a potential cure for HIV.

Next events

Vacc-C5 interim data	Q413
Vacc-4x reboost data	Q114
Vacc-4x Revlimid combo data	Q214
Start of HDI combo trial	2014

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Edison profile page

Investment summary

Company description: Working towards an HIV cure

Bionor Pharma is a Norwegian biotechnology company focusing on the development of peptide vaccines for the treatment of viral infections. Lead product Vacc-4x for the potential treatment of HIV is currently in Phase II trials, with data expected in H114. Vacc-4x has already demonstrated significant HIV viral load reduction and a long-term immune response in previous trials, supporting continued development. Bionor is now working on a comprehensive development strategy, including a collaboration with Celgene and with a leading research institution, which could lead to Vacc-4x as the first potential functional cure for HIV. Through its peptide vaccine technology, Bionor also has a number of earlier-stage candidates in development, which are summarised in Exhibit 1.

Bionor was created in 2010 with Nutri Pharma's acquisition of privately held Bionor Immuno AS. This brought together Nutri Pharma's nutraceutical products and Bionor Immuno's pipeline of peptide-based vaccines. The majority of the nutrition business was sold during 2010 and management plans to either divest or dispose of the remainder by year-end 2013. Bionor had 20 employees at the end of 2012 and new management (CEO and CFO) was appointed in 2013.

Valuation: Risk-adjusted NPV of NOK868m or NOK4.0/share

We value Bionor at NOK868m or NOK4.0/share, based on a risk-adjusted NPV analysis using a 12.5% discount rate. Our rNPV includes Vacc-4x as a potential treatment for HIV, forecasting peak sales of €1.3bn, but we do not include any value for Vacc-C5 given the earlier stage of development and unknown potential magnitude of effect. Together with NOK129m net cash, including NOK54.5m proceeds from the recent private placement, our valuation suggests more than 30% upside to current levels. Our valuation assumes Vacc-4x becomes an additional treatment option for HIV, rather than a replacement treatment to existing anti-retroviral drugs. However, if Vacc-4x is able to functionally cure HIV (ability to control and maintain the virus at undetectable levels without treatment), the peak potential could be significantly larger than our current forecasts as Vacc-4x could attract premium pricing and could treat more patients, leading to peak sales closer to €6-7bn.

Sensitivities: Vacc-4x clinical development success or failure

The main sensitivity for Bionor is the success or failure of lead product Vacc-4x. Although Vacc-4x has already demonstrated a significant reduction of HIV viral load and a long-term immune response, the company still needs to explore how to improve and exploit these characteristics to develop a functional cure. This strategy will require successful outcomes from a number of trials. In addition, Bionor will likely need to partner Vacc-4x to ensure successful commercialisation. Bionor is also subject to the usual biotech risks, which include regulatory, competitor success, financing and commercial risks.

Financials: Cash runway to at least mid-2015

Bionor ended June 2013 with NOK74.8m net cash, which, with the additional NOK54.5m proceeds from the recent private placement, at NOK2.75/share should be sufficient to fund operations to mid-2015 in the absence of any further licensing deals. An additional NOK20.6m could be raised in the proposed issue to shareholders not allocated shares in the private placement, which would extend the cash runway to H215. This would be sufficient to obtain data from the ongoing Vacc-4x reboost study and the ongoing Revlimid combination trial (partially funded by Celgene), which are both due to report during H114, and could potentially allow for data from the planned HDI combo trial. If positive, in our view these data should be sufficient to attract a global Vacc-4x partner.

Outlook: The quest for a cure for HIV

Bionor is focused on the development of peptide vaccines for the treatment of viral infections, with two clinical stage candidates for the potential treatment of HIV. The lead product, Vacc-4x, is currently in Phase II development. In previous clinical trials Vacc-4x demonstrated a significant reduction of HIV viral load and a long-term immune response in infected patients, supporting management's strategy to take Vacc-4x forward as a cure for HIV. This development plan will be shaped and refined by upcoming data from ongoing Phase II trials expected during H114. We value Vacc-4x at NOK 3.4/share based on a 30% probability of global €1.3bn peak sales with a partner paying at least a 15% royalty.

Exhibit 1: Bionor Pharma pipeline

Product	Indication	Stage	Comments
Vacc-4x	HIV therapeutic vaccine	Phase II	Reboost study ongoing; data end-Q114
		Phase II	Revlimid combo; data Q214
		Phase II planning	HDI (romidepsin) combo being planned
Vacc-C5	HIV therapeutic vaccine	Phase I/II	Therapeutic HIV vaccine
Vacc-HIV (Vacc-4x + Vacc-C5)	HIV prophylactic vaccine	Preclinical	GLOBVAC grant to partially fund preclinical and Phase I/II
Vacc-Flu	Flu vaccine	Preclinical	

Source: Bionor Pharma, Edison Investment Research

Both of Bionor's clinical stage vaccine candidates are focused on the treatment of HIV. Each is being developed as a therapeutic vaccine (to treat the disease) rather than prophylactic (preventative) vaccinations. They are also being investigated in a combination as a potential prophylactic vaccine for HIV.

Vacc-4x is in development as a therapeutic vaccine for the treatment of HIV. It targets the conserved p24 region on the HIV-1 virus (the predominant version of HIV) and it is administered intradermally. The vaccine and mode of administration have been designed to elicit a cell-based immune response by generating T-cells (a type of white blood cell). These T-cells consist of both CD4 (helper) and CD8 (killer) cells, which can recognise and destroy infected HIV cells. Vacc-4x has already been investigated in a number of clinical trials, summarised in Exhibit 2.

Exhibit 2: Summary of Vacc-4x clinical development to date

Trial	n	Design	Key findings
Phase I	11	Open label	All patients reported positive DTH responses, an indication of cell-mediated immunity.
Phase IIa	40	Open label	90% DTH response by final immunisation; 62% without ART resumption at month 30; 34% remained off medication at month 44; on average patients remained off ART for 31 months.
Phase IIa-reboost	26	Open label	Immune response enhanced after re-vaccination; active memory response seven years later.
Phase IIb	136	Placebo controlled	Significant reduction of HIV viral load vs placebo; no difference in resumption of cART treatment.

Source: Bionor Pharma, Edison Investment Research. Note: n=number of patients; DTH=delayed-type hypersensitivity, a measure of cell-mediated immunity; ART=antiretroviral therapy; and cART=combination antiretroviral therapy.

Previous Vacc-4x data suggest efficacy against HIV

Most recently Vacc-4x was investigated in a Phase IIb trial in 136 patients. In 2010 the trial was reported as not hitting the primary endpoints and previous management effectively terminated development of Vacc-4x. Only a month later, further examination of the data revealed findings that supported continued development, which current management is now actively pursuing.

Phase IIb trial design: A small but ambitious trial

136 HIV patients that had been stable on ART (antiretroviral therapy) for at least six months with a viral load <50 copies/mL were recruited (126 patients completed). Patients continued to receive ART in combination with either Vacc-4x (93 patients) or placebo (43 patients) over 28 weeks, at which point treatment (including ART) was stopped for up to 24 weeks. ART was resumed if CD4 count dropped below 350 cells/mm^3 or decreased by 50%, or if viral load >300,000 copies/mL.

There were two primary endpoints: the proportion of patients that required resumption of ART in the six months between ART interruption at week 28 and the end of the study at week 52; and the change in CD4 count between week 28 and 'last' CD4 count (defined as either prior to ART resumption or at week 52 if ART was not resumed). Secondary endpoints included HIV viral load and safety and tolerability of Vacc-4x. The trial was started in 2008, with patient recruitment completed by June 2009. Data became available in October 2010.

What the trial did show: HIV viral load reduction

HIV viral load was investigated as a secondary endpoint in the trial. HIV viral load is a measure of the amount of HIV virus in the blood. An 'undetectable' viral load is broadly defined as <50 HIV copies/mL (dependent on the sensitivity of the assay). A high viral load is around >100,000 copies/mL but can be up to 1m copies/mL. A low viral load is less than 200-500 copies/mL.

- **64% viral load reduction vs placebo (p=0.04):** in patients that remained off ART through to week 52, patients treated with Vacc-4x had a viral load set point of 22,300 copies/mL compared with placebo patients with a viral load set point of 61,900 copies/mL. Hence, Vacc-4x reduced viral load by 64% compared to placebo patients (p=0.04). When examining the whole patient population, a statistically significant reduction (p=0.028) was observed.
- **60% reduced viral load compared to pre-ART levels (p=0.0001):** pre-ART viral loads were available for a subset of patients that remained off ART through to week 52. In placebo patients, there was no difference in viral load pre-ART and at study completion (52,731 copies/mL pre-ART and 50,400 copies/mL at study completion, p=0.98). However, there was a 60% reduction in the Vacc-4x arm, with patients going from 60,470 copies/mL pre-ART to 24,150 copies/mL at study completion (p=0.0001). This improved even further to 70% reduced viral load compared to pre-ART levels, with longer-term data in patients followed for another 12 months. This represents >0.5 log reduction, which is considered clinically meaningful by regulators.

What the trial did not show: No difference in ART resumption or CD4 count

The main aim of the trial was to investigate Vacc-4x's potential to delay the need to resume ART treatment. In addition, CD4 count was measured. HIV infects CD4 cells and without treatment, CD4 cell count declines. CD4 cell count is used as a key measure to determine when to initiate treatment, with the US NIH (National Institute of Health) recommending ART treatment is initiated when CD4 count drops below 350 cells/mm^3.

- **No difference in ART resumption:** at week 52 there was a numerical, but not statistical difference, in the number of patients that had resumed ART. In patients that received Vacc-4x 65.9% had not resumed ART by week 52 compared to 71.1% placebo patients (p=0.89).
- **No difference in CD4 counts:** CD4 count was measured from week 28 to either the point at which ART was resumed, or to the end of the trial at week 52. There was no difference between Vacc-4x and placebo, with CD4 counts declining 36.0% in Vacc-4x treated patients compared to 30.3% CD4 count reduction in the placebo group (p=0.12).

Deciphering the data

There are a number of potential reasons why Vacc-4x was able to reduce viral load without hitting either of the primary endpoints:

- **Six-month treatment interruption too short:** the duration of treatment interruption in the Phase IIb trial was a maximum of six months (from week 28 when treatment was stopped, to the trial completion at week 52). Longer-term data from this, and from other trials, potentially suggest that six months without ART may not be long enough to necessitate treatment

resumption, even in placebo patients: (1) data from patients in the trial followed for an additional 12 months demonstrated that 30% of Vacc-4x patients had remained off ART treatment, almost double the 18% of placebo patients, ie over a longer time point a difference was seen; (2) in a previous 40-patient Phase IIa trial, patients treated with Vacc-4x stayed off ART for an average of 31 months; and (3) in the NIH's SMART study (Strategies for Management of Antiretroviral Therapy), the largest trial specifically investigating ART interruption strategies in 5,792 patients, the median duration of first treatment interruption was 16.8 months (range 5.7 to 42.3) – although not directly comparable, this group of patients might be considered broadly similar to the placebo arm in Vacc-4x's Phase IIb trial.

- **Trial size too small:** the principle investigator in the Phase IIb trial suggested that the trial may have failed as too few people took part. Examining HIV trials investigating structured treatment interruption (STI), conflicting data have been reported, with the SMART study (n=5,492) and the Trivican study (n=326) suggesting that STI has a detrimental effect (the SMART study was terminated early as patients in the STI arm had twice the risk of disease progression). The Staccato study (n=430) suggested a potential benefit of STI. These are all larger studies than Bionor's Phase IIb with conflicting conclusions, perhaps suggesting that ART interruption/resumption is not necessarily a straightforward measure.
- **CD4 quality but not quantity improved:** as HIV replicates, infects and destroys CD4 cells, viral load will typically increase and CD4 count will decrease. Conversely, viral load suppression is associated with a higher CD4 count, indicating a healthy immune system. Vacc-4x did reduce viral load more than placebo, but this was not associated with an increase in CD4 count. It may be that the viral load was not reduced enough to see the consequent increase in CD4. Perhaps more importantly, patients vaccinated with Vacc-4x appeared to have a better quality immune response, which could explain why the viral load reduced.

Vacc-4x: 'Kick, Kill and Boost' to cure HIV

The previous clinical data support continued development of Vacc-4x as a treatment for HIV, owing to viral load reduction and quality of immune response. With these data Bionor has developed a comprehensive strategy to take Vacc-4x forwards as a potential functional cure for HIV. Data from ongoing trials will help shape and determine future development, likely in collaboration with a partner. A functional cure maintains virus at undetectable levels without treatment. This strategy involves three key elements, referred to as 'Kick, Kill and Boost'. All of these will need to be successful for an effective functional HIV cure:

- **Kick:** in the early stages of HIV infection, so-called latent reservoirs are established. These do not actively produce HIV and are effectively invisible to ART. However, if ART treatment is stopped, these reservoirs are reactivated, producing HIV. Hence, ART cannot cure HIV. Recent research conducted at the Aarhus University Hospital in Denmark suggests that HDIs (histone deacetylase inhibitors) can reactivate or kick awake these latent reservoirs. Bionor is planning a Vacc-4x combination trial with romidepsin (Istodax, Celgene) with the Aarhus University, which is leading research into HDIs to reactivate latent reservoirs. This could start in 2014.
- **Kill:** previous trials have already demonstrated viral load reduction with Vacc-4x, suggesting Vacc-4x is able to induce HIV destruction via T-cell mediated immunity. An ongoing trial is investigating reboosting patients with Vacc-4x to determine if additional vaccination can induce further viral load reduction, with data expected in Q114. Immune response and viral load reduction compared to the previous study are being measured. If this is successful, re-boosting will be considered in future combination trials.
- **Boost:** the very mechanism of HIV infection affects and weakens the immune system. Vacc-4x relies on a functioning immune system to destroy HIV. Hence, improving the immune system's ability to fight HIV could improve Vacc-4x's efficacy. As part of a research collaboration with Celgene, a trial combining Vacc-4x with Revlimid (lenalidomide, Celgene's immune modulator,

likely to be off-patent by the time of Vacc-4x's launch) is ongoing, with data anticipated in Q214. The trial will measure CD4 count and T-cell response, among others, as a measure of immune system response.

Is curing HIV even possible?

Following the first reports of AIDS in 1983, current treatment for HIV centres on the use of combining anti-retroviral drugs (cART) that target different stages of the HIV life cycle. ART is able to suppress viral replication but if cART is discontinued, viral load rebounds. Alternatives to cART have been attempted, but many have failed, including prophylactic vaccine approaches (Exhibit 3). However, the case of the Berlin Patient suggests that curing HIV is possible.

Timothy Brown (the Berlin Patient) was diagnosed with HIV in 1995 and was treated with ART. However, in 2006 Brown developed leukaemia and needed a bone marrow transplant. Brown's physicians opted to search for a donor with a specific genetic mutation known as CCR5-Δ32. CCR5 is used by HIV to enter and infect host cells and a Δ32 mutation leads to natural HIV resistance, meaning a carrier cannot be infected with HIV. Around 1% of the EU population are estimated to carry this mutation. Timothy Brown received a bone marrow transplant from a donor carrying the CCR5-Δ32 mutation in 2007 and has been functionally cured of HIV since, with no detectable HIV.

Vacc-4x is one of the most advanced therapeutic vaccines

ART treatment has evolved over the past 25 or so years, with today's combination therapy (cART) reducing morbidity and mortality, and HIV patient life expectancy is now almost that of the general population. However, long-term treatment with ART does have health complications, including cardiovascular disease and kidney, liver and bone effects. CDC (Centres for Disease Control) estimates that only 25% of US patients are fully virally suppressed, and literature and clinical experience suggest that only around 65% of HIV patients are 100% adherent after eight months of ART treatment, with compliance worsening with treatment duration. There is a concern that drug resistant strains of HIV could emerge. Hence, there remains a need for novel, alternative options to ART.

HIV vaccine development has been challenging

The very nature of HIV infection makes HIV vaccine development challenging. Vaccines rely on the immune system; however, HIV infection directly affects and weakens the immune system. According to the WHO (World Health Organisation), around 30 vaccine candidates have been tested in over 80 Phase I/II clinical trials. Only a handful of Phase III trials have been conducted globally, but none have yielded data sufficient for approval. A summary of selected prior HIV vaccine development is in Exhibit 3.

Exhibit 3: Selected HIV vaccine development to date

Product	Company	Trial	Start/end	n	Overall conclusion	Data
AIDSVAX	VaxGen	US Phase III	Start 1998, complete 2003	5,403	Vaccine did not protect against HIV-1	Annual incidence of infection 2.7% in both arms; infection rates were 6.7% in AIDSVAX arm and 7.0% on placebo.
		Thai Phase III	Start 1999, complete 2003	2,546	Vaccine did not protect against HIV-1	Annual incidence of infection 3.4% in both arms; infection rates were 8.4% in AIDSVAX arm and 8.3% on placebo.
ALVAC-HIV + AIDSVAX	Sanofi + VaxGen	RV 144 Phase III trial	Start 2003, data 2009	16,395	Vaccine reduced HIV infection by 31.2% compared with placebo; 2011 reanalysis: 29% chance that the vaccine was not effective	74 placebo HIV infections vs. 51 vaccine (p=0.04).
V520	Merck	Phase II STEP	Start 2004, terminated 2007	3,000	Vaccine could neither prevent HIV infection nor reduce the amount of virus in those who became infected with HIV.	49 HIV infection cases on vaccine vs 34 cases of HIV infection on placebo, suggesting the vaccine increased susceptibility to infection.

Source: Edison Investment Research

Despite the failure of many vaccine candidates the search for an HIV vaccine continues, with estimates suggesting that global R&D investment since 2001 has totalled $8bn, with $845m invested in 2011. The Berlin Patient has reinvigorated research into an HIV cure, particularly among therapeutic vaccine developers, and Bionor's Vacc-4x is one of the most advanced. A summary of selected later-stage therapeutic vaccines is shown in Exhibit 4.

Exhibit 4: Selected clinical stage HIV therapeutic vaccines

Product	Company	Stage	Type	Key data to date
Vacc-4x	Bionor Pharma	Phase IIb	Peptide T-cell vaccine targeting p24	64% viral load reduction vs placebo (n=136)
AGS-004	Argos Therapeutics	Phase IIb	Personalised dendritic cell-based immunotherapy	ART + AGS-004 induced HIV-specific CD8 T-cell response (n=10)
DCV-2	Hospital Clinic of Barcelona	Phase II	Personalised dendritic cell-based immunotherapy	90% viral load set-point reduction in 55% patients at wk 12 post ART interruption; wk 48 only 15% vaccinated patients still had viral load suppression (n=36)
DermaVir patch	Genetic Immunity	Phase II	Synthetic HIV-like nanomedicine	Long lasting T-cell increase from pre-treatment in dose dependent manner (n=9)
FIT-06	FIT Biotech	Phase II	Recombinant plasmid DNA HIV-1 vaccine	0.47 log viral load reduction (p=0.001) at 108 weeks (n=60). CD4 count increased 72 cells/ml (p=0.013) (patients not previously treated with ART)
732462	GlaxoSmithKline	Phase II	Fusion protein	ND; long-term follow-up to prior Phase II investigating viral load change at wk 48 in ART naive patients
HIV-1 Tat vaccine	Italian National Institute of Health	Phase II	Tat-based vaccine (tat is a key HIV regulatory gene)	Phase I preventative and therapeutic trials confirmed safety and immunogenicity

Source: Edison Investment Research

Vacc-4x could generate peak sales of €1.3bn ($1.7bn)

In 2012, the HIV market generated sales of nearly $17bn from the sale of ART (a summary of key treatment options is shown in Exhibit 5). Despite significant sales, according to the CDC, of the 1.1 million Americans with HIV in the US only 33% are prescribed ART, of which c 75% are virally suppressed. HIV patients treated with ART face a lifetime of daily pills, often with severe side-effects and long-term health implications. Hence, there is a sizeable market for new treatments.

Exhibit 5: Summary of current ART (antiretroviral therapy) HIV treatment

Drug Class	Main drugs	Approx. 2012 WW sales	Mechanism of action
Multi-class	Atripla (Gilead) Stribild (Gilead, approved Aug 12)	$4bn	Combination of various drug classes.
Protease inhibitors (PIs)	Kaletra (AbbVie) Prezista (J&J) Rayataz (BMS)	$4.5bn	PIs prevent viral replication by specifically targeting viral protease enzymes. Blocking activity of these enzymes prevents the long protein strands produced within the host CD4 cell from being cut up into the smaller proteins needed for functional HIV particles.
Nucleoside/Nucleotide Reverse Transcriptase Inhibitors (NRTIs/NtRTIs)	Truvada (Gilead, NRTI combo) Epzicom (ViiV, NRTI combo)	$6bn	HIV RNA must be converted to DNA via reverse transcription in order to be incorporated into the host CD4. NRTIs (nucleoside analogues or 'nukes') and NtRTIs aim to gatecrash building of the viral DNA chain by inserting faulty nucleotides (building blocks), which terminate viral DNA synthesis.
Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)	Sustiva (BMS) Intelence (J&J)	$0.5bn	NNRTIs (non-nucleosides or 'non-nukes') target viral reverse transcription. NNRTIs bind to the reverse transcriptase enzyme to stop it from working properly.
Other	Isentress (Merck) Tivicay (ViiV, approved Aug 13)	$2bn	Fusion inhibitors, entry inhibitors, integrase inhibitors.
		$17bn	

Source: Edison Investment Research

Base-case scenario: Vacc-4x as an alternative HIV treatment

Our base-case model assumes that Vacc-4x is positioned as an alternative to ART, rather than as a replacement or cure. Clinical data to date demonstrate Vacc-4x can significantly decrease viral load, which is supportive of Vacc-4x in this setting. We assume that Vacc-4x is able to penetrate around 20% of the c 90,000 US patients that despite receiving ART are not virally suppressed, implying <2% Vacc-4x penetration of the overall US HIV market.

Previous data suggest that Vacc-4x could prevent the need for ART for an extended period. If Vacc-4x can show in further trials that it can safely preclude the need for ART for an extended period of time (at least 12 months), this could provide an attractive treatment option. The length of ART 'holiday' will likely be one of the key variables in determining pricing. We estimate that a one- to two-year ART holiday would justify around a 40% premium to the current most convenient treatment option, Stribild, which is a multi-class once-a-day pill combining four therapies, and is priced at $28,500 per year (the wholesale acquisition cost).

Based on these patent and pricing assumptions we arrive at peak sales of €1.3bn in the US and developed EU, which we assume would be around six years post-launch.

Best-case scenario: Vacc-4x as a functional HIV cure

If Vacc-4x is successfully developed as a functional cure for HIV, then we estimate peak sales could be substantially higher than our base case forecasts. Pricing could more likely be closer to cancer immunotherapy type levels (Provenge is priced at around $90k). Furthermore, there could be a larger patient pool that receives Vacc-4x. As an immunotherapy, it is possible that Vacc-4x will be most effective in a specific subset of patients (yet to be fully determined but will become clearer in later-stage trials). However, it is possible that Vacc-4x could treat double the amount of patients treated in our base-case scenario. With premium pricing, this would suggest peak sales of €6.5bn.

Solid patent protection until at least 2020

The Vacc-4x composition of matter type patents should provide protection until at least March 2020, without extensions. If Vacc-4x is commercially launched, it will also benefit from data exclusivity (12 years in the US for vaccines and eight years in Europe).

Vacc-C5 provides another HIV treatment candidate

Bionor is also developing Vacc-C5, which aims to generate an antibody immune response (in contrast to Vacc-4x, which elicits a cell-mediated T-cell response). <5% of HIV patients are natural viral suppressors (also referred to as long-term non-progressors, LTNP or elite controllers) that can control HIV without the need for medication. LTNP have been found to have antibodies to C5, a preserved region on the HIV surface glycoprotein gp120. Vacc-C5 has been developed to induce antibodies to this region.

Vacc-C5 is currently being investigated in a Phase I/II trial to investigate safety and antibody response and data are expected during Q114. Interim data from this open label trial could be available before the end of 2013. The results from this trial will help determine the future development of Vacc-C5, which could either be as a monotherapy as a therapeutic vaccine, or potentially in combination with Vacc-4x as a potential prophylactic vaccine.

We do not include Vacc-C5 in our valuation owing to the lack of proof-of-concept data. Hence, Vacc-C5 represents pure upside to our current estimates and forecasts.

Vaccine technology platform to feed the pipeline

Bionor's peptide vaccine technology is used to modify peptides (small protein chains) that have been selected to target specific regions on a virus that do not change, even in new viral strains. Once a conserved viral region has been identified, Bionor selects a peptide to target it with the aim of triggering an immune response. In contrast to traditional vaccines such as smallpox, peptide vaccines do not contain any part of the virus (either whole or partial), inactivated (killed) or attenuated (live, but weakened). The absence of virus containing material in a peptide vaccine reduces the risk of virulence (reversion to a virulent, disease causing form). In addition, peptides can be simpler to manufacture at lower cost. While peptide vaccines may not evoke as strong an

immune response as a traditional vaccine, Bionor's peptide modification technology (amino acid substitution) is designed to enhance the immune response.

Sensitivities

Bionor is subject to the usual biotech risks, including clinical development delays or failures, regulatory risks, competitor successes, partnering setbacks, financing and commercial risks. The main near-term sensitivity for Bionor is the success or failure of Vacc-4x. For Vacc-4x to be successfully commercialised as a treatment for HIV, it will likely require improved HIV viral load reduction and CD4 cell count increases. Previous HIV vaccine development has been challenging and, despite around two decades of research, no HIV vaccine has been successfully developed. However, prior development has tended to focus on prophylactic vaccines, unlike Vacc-4x, which is being developed as a therapeutic vaccine.

For Vacc-4x to be commercialised as a functional HIV cure, all elements of the "Kick, Kill and Boost" strategy will need to be successful, which is not without risk. Furthermore, the development path is largely unknown. While the FDA has published detailed and comprehensive guidelines on the development of ART for HIV, there are no guidelines, to our knowledge, that outline clinical trial design or endpoints for a functional cure. This means that potential development timelines are largely unknown. We have assumed Vacc-4x launch in 2019, allowing a further five to six years of clinical development. However, regulatory requirements could potentially delay this beyond our forecasts.

In terms of other regulatory risks, Vacc-4x is administered with GM-CSF (granulocyte-macrophage colony-stimulating factor) as an adjuvant (to enhance the immune system's response to a vaccine). To our knowledge, GM-CSF has not been approved as an adjuvant by regulators.

The clinical development and successful commercialisation of Vacc-4x is likely to be expensive, which a partner could facilitate. However, we have limited visibility on the potential timing or terms of any partnership. Executing a deal will likely depend on the strength of the clinical data.

Vacc-4x is one of the most advanced therapeutic vaccine candidates in development. However, there are a number of competitor products in clinical development. If a competitor is able to progress development more swiftly, or can show better efficacy or safety, this could reduce the potential market for Vacc-4x.

Following the recent private placement, we estimate Bionor has around NOK129m net cash, which could be bolstered by an additional NOK20.6m from the proposed offer to shareholders not allocated shares in the private placement. If this issue is successfully executed as planned, our model and estimates suggest cash should be sufficient to fund operations to H215 in the absence of any licensing deals. Any further capital raises would likely be a dilutive financing event.

Valuation

We value Bionor at NOK868m or NOK4.0/share, based on a risk-adjusted NPV analysis, which includes NOK129m net cash, including NOK54.5m proceeds of the recent private placement at NOK2.75/share, but not the proposed NOK20.6m issue. The breakdown of our rNPV valuation, which uses a 12.5% discount rate, is shown in Exhibit 6. Our valuation includes only Vacc-4x, with no value assigned to Vacc-C5 or the preclinical pipeline, given their earlier stage of development and lack of proof-of-concept data.

The outcome of upcoming data from the ongoing and planned Vacc-4x trials will be key for our valuation, with data expected during Q114 from the reboost trial and Revlimid combo data expected

during Q214. Depending on the precise outcome, these data could be worth an additional NOK1/share if positive, based on an increased 40% Vacc-4x probability of success.

Exhibit 6: Bionor Pharma rNPV valuation

Product	Indication	Launch	Peak sales (€m)	Value (NOKm)	Probability	rNPV (NOKm)	NPV/share (NOK/share)
Vacc-4x	Therapeutic HIV vaccine	2019	1,300	2,461.3	30%	738.4	3.4
Net cash/(debt)				129.3	100%	129.3	0.6
Valuation				**2,590.6**		**867.6**	**4.0**

Source: Edison Investment Research

Although Vacc-4x is being developed as a functional cure for HIV, its potential profile in this setting is still being established. Hence, we more prudently base our valuation on our base-case scenario of €1.3bn peak sales in 2025, assuming launch in 2019. We assume that Bionor will seek to partner Vacc-4x from H215, once data from the ongoing reboost and Revlimid combo trials are available, and potentially data from the planned HDI combo trial. We assume that a global partner will cover all development costs, paying at least a 15% royalty on global sales. We assign a 30% probability of success, which is broadly in line with industry standards for a Phase II asset with proof-of-concept data.

Vacc-4x as a cure implies a valuation of NOK5.6/share based on 10% probability

Our best-case peak sales scenario of €6.5bn if Vacc-4x is developed as a functional cure would offer significant upside to our base-case valuation. However, a lower probability of success would be appropriate, given there remain a number of uncertainties with this strategy, including the efficacy of Vacc-4x combined with an HDI, and the unknown development path that might be required by regulators. A 10% probability of €6.5bn sales would suggest a Vacc-4x valuation of NOK5/share, or NOK5.6/share for the company, including NOK129m (NOK0.6/share) net cash.

Financials

Bionor reported NOK74.8m net cash at end-June 2013, which together with the NOK54.5m private placement at NOK2.75/share should be sufficient to fund operations to mid-2015, according to our model. A potential NOK20.6m issue for shareholders that were not allocated shares in the private placement has been proposed and could be executed in the near term, which would extend the cash runway into H215.

Our 2013 revenue forecast includes NOK2.7m nutraceutical sales, although management plans to either dispose or discontinue this business by the end of the year. Hence our forecasts beyond 2013 do not include any contribution from this segment, with revenues from 2014 including only a small contribution from sales in the Vaccine segment (NOK1.6m in 2012).

Bionor's expenses are classified according to nature (personnel and other) rather than by function (R&D, SG&A), although R&D spend is disclosed in the annual report. We expect R&D spend to increase slightly from NOK26.8m in 2012 over the next three years, with the ongoing Vacc-4x reboost trial, the Revlimid combo study (costs shared with Celgene) and the planned HDI combo Vacc-4x trial. Beyond 2016, we assume Vacc-4x R&D spend will be assumed by a partner. Our operating expenses in 2013 are NOK77.1m, in line with guidance of NOK70-80m.

Our forecasts include illustrative financing in 2015 of NOK24.3m, which we class as a long-term liability for the purposes of our model. Successfully executing the proposed NOK20.6m issue will reduce this financing need. Additionally, any Vacc-4x partnership could include an upfront payment, which would delay the need for further financing.

Exhibit 7: Financial summary

NOK000s	2009	2010	2011	2012	2013e	2014e	2015e
December	IFRS	IFRS	IFRS	IFRS	IFRS	IFRS	IFRS
PROFIT & LOSS							
Revenue	20,668	12,591	109,499	4,224	4,287	1,603	1,619
Cost of Sales	(9,300)	(762)	(1,605)	(1,864)	(1,864)	(19)	(19)
Gross Profit	11,368	11,829	107,894	2,360	2,423	1,584	1,599
Research and development	(389)	(18,900)	(22,700)	(26,800)	(28,324)	(28,803)	(29,331)
EBITDA	2,675	(35,247)	57,357	(58,221)	(60,988)	(63,527)	(65,365)
Operating Profit (before amort. and except.)	2,579	(35,654)	56,833	(58,903)	(61,919)	(64,485)	(66,337)
Intangible Amortisation	(257)	(8,817)	(10,776)	(10,776)	(10,776)	(10,776)	(10,776)
Exceptionals	0	0	0	0	0	0	0
Other	2,874	(3,692)	(1,460)	(792)	0	0	0
Operating Profit	5,196	(48,163)	44,597	(70,471)	(72,695)	(75,261)	(77,113)
Net Interest	116	711	4,423	3,706	1,576	1,182	77
Profit Before Tax (norm)	2,695	(34,943)	61,256	(55,197)	(60,343)	(63,303)	(66,260)
Profit Before Tax (FRS 3)	5,312	(47,452)	49,020	(66,765)	(71,119)	(74,079)	(77,036)
Tax	0	(3)	0	0	0	0	0
Profit After Tax (norm)	2,587	(38,638)	59,796	(55,989)	(60,343)	(63,303)	(66,260)
Profit After Tax (FRS 3)	5,312	(47,455)	49,020	(66,765)	(71,119)	(74,079)	(77,036)
Average Number of Shares Outstanding (m)	86.5	168.3	180.5	190.3	208.4	218.3	218.3
EPS - normalised (NOK)	0.03	(0.23)	0.33	(0.29)	(0.29)	(0.29)	(0.30)
EPS - normalised and fully diluted (NOK)	0.03	(0.23)	0.33	(0.29)	(0.29)	(0.29)	(0.30)
EPS - (IFRS) (NOK)	0.06	(0.28)	0.27	(0.35)	(0.34)	(0.34)	(0.35)
Dividend per share (p)	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Gross Margin (%)	55.0	93.9	98.5	55.9	56.5	98.8	98.8
EBITDA Margin (%)	12.9	-279.9	52.4	-1378.3	-1422.7	-3964.1	-4038.3
Operating Margin (before GW and except.) (%)	12.5	-283.2	51.9	-1394.5	-1444.4	-4023.8	-4098.4
BALANCE SHEET							
Fixed Assets	4,084	115,383	101,593	93,159	81,667	70,013	58,346
Intangible Assets	3,494	113,713	99,712	88,936	78,160	67,384	56,608
Tangible Assets	122	1,192	1,403	3,288	2,572	1,694	803
Investments	468	478	478	935	935	935	935
Current Assets	15,634	64,868	151,802	115,319	115,289	55,174	16,420
Stocks	0	0	0	0	0	0	0
Debtors	2,524	4,261	76	85	88	44	67
Cash	11,911	57,851	144,106	108,881	108,848	48,777	10,000
Other	1,199	2,756	7,620	6,353	6,353	6,353	6,353
Current Liabilities	(1,264)	(19,048)	(47,210)	(15,573)	(18,656)	(18,902)	(19,177)
Creditors	(1,264)	(13,228)	(41,249)	(12,708)	(18,656)	(18,902)	(19,177)
Short term borrowings	0	(5,820)	(5,961)	(2,865)	0	0	0
Long Term Liabilities	0	(8,472)	(2,865)	0	0	0	(24,276)
Long term borrowings	0	(8,472)	(2,865)	0	0	0	(24,276)
Other long term liabilities	0	0	0	0	0	0	0
Net Assets	18,454	152,731	203,320	192,905	178,300	106,285	31,313
CASH FLOW							
Operating Cash Flow	6,651	(43,108)	(41,069)	(56,646)	(52,979)	(61,173)	(63,049)
Net Interest	1	(622)	(3,975)	3,069	1,576	1,182	77
Tax	0	0	0	0	0	0	0
Capex	(17)	(20)	(735)	(2,769)	(214)	(80)	(81)
Acquisitions/disposals	0	0	110,000	0	0	0	0
Financing	6,750	75,398	27,500	27,082	54,450	0	0
Dividends	0	0	0	0	0	0	0
Net Cash Flow	13,385	31,648	91,721	(29,264)	2,832	(60,071)	(63,053)
Opening net debt/(cash)	1,474	(11,911)	(43,559)	(135,280)	(106,016)	(108,848)	(48,777)
HP finance leases initiated	0	0	0	0	0	0	0
Other	0	0	0	0	(0)	0	0
Closing net debt/(cash)	(11,911)	(43,559)	(135,280)	(106,016)	(108,848)	(48,777)	14,276

Source: Bionor Pharma accounts, Edison Investment Research

EDISON

Contact details	Revenue by geography
Bionor Pharma ASA Kronprinsesse Märthas plass 1 NO-0116 Oslo Norway +47 23 01 09 60 www.bionorpharma.com/en	N/A

CAGR metrics		Profitability metrics		Balance sheet metrics		Sensitivities evaluation	
EPS 2010-14e	N/A	ROCE 2013e	N/A	Gearing 2013e	N/A	Litigation/regulatory	●
EPS 2012-14e	N/A	Avg ROCE 2010-14e	N/A	Interest cover 2013e	39.3	Pensions	○
EBITDA 2010-14e	N/A	ROE 2013e	N/A	CA/CL 2013e	6.2	Currency	◖
EBITDA 2012-14e	N/A	Gross margin 2013e	56.5%	Stock days 2013e	N/A	Stock overhang	◖
Sales 2010-14e	(40.3%)	Operating margin 2013e	N/A	Debtor days 2013e	7.5	Interest rates	○
Sales 2012-14e	(38.4%)	Gr mgn / Op mgn 2013e	N/A	Creditor days 2013e	100	Oil/commodity prices	○

Management team

CEO: Anker Lundemose	CFO: Synne Røine
Mr Lundemose joined Bionor in March 2013 as president and CEO. He has significant senior management experience in the healthcare sector across a range of companies, from biotech start-ups to large biotech and big pharma. Most recently he was executive vice president, corporate and business development at OSI until its 2010 acquisition by Astellas. Mr Lundemose is a medical microbiologist and holds a PhD, MD and DMSc.	Ms Røine joined Bionor as CFO in May 2013, having previously held the position of CFO at Pronova BioPharma since 2009 until its acquisition by BASF in January 2013. Ms Røine worked at Pronova since 2005, and was involved in the financial team during the 2007 IPO. Ms Røine holds a Master's degree in business administration from Université des Sciences Sociales, Toulouse, France.
Head of development: Vidar Wendel-Hansen	**Chairman of the board: Lars Høie**
Mr Wendel-Hansen joined Bionor in January 2011 from Gilead, where he was medical director for the Nordic and Baltic regions. He has over 15 years of biotech and pharma industry experience, both in preclinical and clinical research and development. Mr Wendel-Hansen holds a PhD and MD.	Mr Høie was elected chairman of the board of directors in 2011. He co-founded Nutri Pharma in 1993. Mr Høie is an MD, holds a PhD in protein and lipid research and has published several papers. Mr Høie has been investing in biotech for more than a decade and is the major shareholder of Bionor Pharma.

Principal shareholders	(%)
Lars H Høie C/O Seb Priv Bank	18.41
Skandinaviska Enskil Meglerkonto Innl.	9.97
Delphi Norge Jpmorgan Europe Ltd	2.33
Kalda As	2.18
Dukat As	2.07
Trond Syvertsen	1.83
Arctic Funds Plc Bny Mellon Sa/Nv	1.81
Franoco As	1.67

Companies named in this report

AbbVie (ABBV US), Argos Therapeutics (private), Bristol-Myers Squibb (BMY US), Celgene (CELG US), FIT Biotech (private), Genetic Immunity (private), Gilead (GILD US), GlaxoSmithKline (GSK LN), J&J (JNJ US), Merck (MRK US), Sanofi (SAN FP), VaxGen (private)

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