EDISON

Photocure

Initiation of coverage

Seeing the light

Pharma & biotech

Photocure is a commercial-stage Norwegian speciality pharmaceutical company that currently markets Hexvix/Cysview, an optical imaging agent for diagnosing and managing bladder cancer. The franchise is currently profitable and sales are growing at an annualised rate of 38%. The company is Phase III-ready for Cevira, a treatment for HPV-related diseases of the cervix, and for Visonac, for moderate to severe inflammatory acne. We value Photocure at NOK1,523m or NOK71/share.

Year end	Revenue (NOKm)	PBT* (NOKm)	EPS* (NOK)	DPS (NOK)	P/E (x)	Yield (%)
12/14	129.0	1.5	0.07	0.0	N/A	N/A
12/15e	129.7	(16.4)	(0.76)	0.0	N/A	N/A
12/16e	151.6	(1.8)	(0.08)	0.0	N/A	N/A
12/17e	170.4	9.9	0.45	0.0	82.0	N/A

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

Hexvix/Cysview: A profitable, growing base business

Hexvix/Cysview is approved globally for detecting and managing bladder cancer. It improves detection rates and helps prolong recurrence-free survival. Growth is currently being driven mainly in the US, although the launch has been slow due to reimbursement issues and the need to purchase a specific blue-light device for use with the product. The company has initiated a Phase III trial for the purpose of label expansion into the surveillance segment, which has the potential to expand the market opportunity twofold to threefold. Results are expected in 2017.

Cevira: Helping to stop cancer before it starts

Cevira is an integrated combination of a drug with an intra-vaginal device for the treatment of patients with HPV-related diseases of the cervix. It has demonstrated statistically significant efficacy in patients with high-grade squamous intraepithelial lesions (HSIL), which has over one million cases diagnosed annually in the US and EU and indicates a higher risk of cancer. Photocure recently announced the approval of its Special Protocol Agreement (SPA) with the FDA for the registration programme.

Visonac: Providing a safer alternative for acne

Visonac may be the first photodynamic treatment for inflammatory acne and could be used for those who fail or are unsuitable for isotretinoin and oral antibiotics, a two million-person market in the US and EU. Phase IIb data were promising, with efficacy in line or better than Solodyn, a leading treatment for moderate to severe inflammatory acne. It is currently Phase III-ready with an SPA.

Valuation: NOK71 per basic share

We value Photocure at NOK1,523m or NOK71 per basic share (NOK67 per diluted share). Upcoming catalysts will be the commencement of enrollment for the Phase III for Hexvix/Cysview to expand into the surveillance market and potential partnerships for both Visonac and Cevira.

25 September 2015

Price	**NOK36.90**
Market cap	**NOK790m**
	NOK8.4/US$
Net cash (NOKm) at end Q215	147
Shares in issue	21.4m
Free float	82.3%
Code	PHO
Primary exchange	Oslo
Secondary exchange	N/A

Share price performance

%	1m	3m	12m
Abs	(0.8)	0.5	76.6
Rel (local)	(1.8)	17.6	101.7
52-week high/low	NOK43	NOK18	

Business description

Photocure specialises in photodynamic therapy. Its bladder cancer imaging product is sold as Hexvix in Europe and Cysview in the US. Photocure handles the marketing in Nordic countries and the US, while Ipsen is its marketing partner in the EU. Cevira is a Phase III-ready product for HPV-related diseases of the cervix and Visonac is a Phase III-ready product for acne.

Next events

Commence enrollment Hexvix/Cysview surveillance trial	H215
Partnerships for Cevira and Visonac	2016

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Investment summary

Company description: A profitable foundation to build on

Photocure is a photodynamic therapy company that was founded by the Norwegian Radium Hospital in 1997 and listed on the Oslo Stock Exchange in 2000. It received its first approval in 2001 for Metvix, a photodynamic therapy for skin cancers, which was first licensed and then sold to Galderma.

It currently markets the imaging agent known as Hexvix in the EU and Cysview in the US, which is approved globally for detecting and managing bladder cancer. It improves detection rates and helps prolong recurrence-free survival. The company recently announced the approval of its SPA by the FDA for the registration programme for Cevira, which is an integrated drug/device combination for the treatment of patients with HPV-related diseases of the cervix. It has demonstrated statistically significant efficacy in patients with high-grade squamous intraepithelial lesions (HSIL), which has over 1m cases diagnosed annually in the US and EU and indicates a higher risk of cancer. Visonac is its Phase III-ready treatment for inflammatory acne, which could be used in those who fail or are unsuitable for isotretinoin and oral antibiotics, a two million-person market in the US and EU.

Valuation: NOK71 per basic share

Using a risk-adjusted NPV model with a 10% discount rate for Hexvix/Cysview and 12.5% for Cevira and Visonac, we arrive at a value for Photocure of NOK1,523m or NOK71 per basic share (NOK67 per diluted share). As the company has indicated that it is seeking partners to continue the development of both Cevira and Visonac, we have assumed that it will receive a 17.5% royalty rate, as well as milestones for both products.

Financials: Improving Hexvix/Cysview profitability

The Hexvix/Cysview franchise is profitable, with NOK14.1m in operating profits in H115, compared to NOK8.7m in the previous year. US revenue is the main growth driver as it is up 117% so far this year compared to last year. With NOK146.7m in cash and the possibility for upfront and regulatory milestone payments, Photocure should have enough capital to meet its needs

Sensitivities: Patent, development and regulatory risk dominate

Photocure is subject to various sensitivities common to pharmaceutical product companies, including development, commercialisation, competitive, reimbursement and patent expiration risks. Hexvix/Cysview is growing very well in the US and could potentially have a surge in sales following approval for the surveillance market, expected around 2018, but its patent runway is short. Patent protection expires in the EU in September 2019 and in the US in November 2020 (however, we assume there are residual sales due to the drug/device combination nature of Hexvix/Cysview). Also, the current major impediments to Hexvix/Cysview adoption in the US are not likely to be resolved any time soon, namely poor reimbursement, the need to purchase a specific and expensive blue-light device for use with the product and inadequate sales/marketing support for the product. With regard to Cevira, it is a relatively high-risk programme as its proof of efficacy comes from a small subgroup within a larger trial. Also, there are competitive excisional and ablative procedures that are very efficacious, quick and relatively inexpensive, although some do increase the lifetime risk of preterm labour. Finally, the company has said the programme will not progress before a partnership is signed. For Visonac, while data have been promising and it also has an SPA with the FDA, it has been Phase III-ready since 2013 as the company has sought a partner which leads one to question whether potential partners agree on its market potential due to the fact that it requires four visits to a physician's office for close to two hours each over the course of six weeks.

Expanding the use of photodynamic therapy

Photocure is currently focused on the development and commercialization of three products (see Exhibit 1). It currently markets Hexvix/Cysview, which is approved globally for detecting and managing bladder cancer. Clinical studies have shown that it consistently helps improve recurrence-free survival compared to the standard of care. Cevira is a drug/device combination for the treatment of patients with HPV-related diseases of the cervix. It appears effective in HSIL, which has more than one million cases diagnosed annually in the US and EU and indicates a higher risk of cancer. Visonac is its Phase III-ready photodynamic treatment for inflammatory acne, which could be used in those who fail or are unsuitable for isotretinoin and oral antibiotics, a two million-person market in the US and EU.

Exhibit 1: Photocure pipeline

Product	Active Ingredient	Indication	Stage	Upcoming catalyst	Advantages over currently approved products
Hexvix/Cysview	Hexaminolevulinate hydrochloride (HAL)	Detection and management of bladder cancer	Market	Commencement of enrollment of surveillance trial	Improves ability to see cancerous lesions on the bladder. Improves recurrence-free survival
Cevira	Hexaminolevulinate hydrochloride (HAL)	HPV-related diseases of the cervix	Phase III	Partnership potentially in 2016	Lower pre-term labour risk than surgical procedures
Visonac	Methyl aminolevulinate (MAL)	Moderate-to-severe inflammatory acne	Phase III	Partnership potentially in 2016	Potential efficacy in refractory patients

Source: Photocure

Hexvix/Cysview for bladder cancer imaging

Hexvix/Cysview hexaminolevulinate hydrochloride is a marketed colourless contrast solution, hexaminolevulinate hydrochloride (HAL), indicated for the detection of non-muscle invasive papillary bladder cancer as part of the transurethral resection of the bladder (TURB) procedure. The solution is administered into the bladder before cystoscopy (a cystoscope is a thin tube with a lighted tip). It then takes about an hour for it to be absorbed into the urinary epithelial cells and accumulates in rapidly growing cells like cancer cells. Using a blue light cystoscope, cancerous tissue would appear to be bright pink/red. Historically, doctors would shine just a white light onto the bladder to see any cancerous tissue, but unfortunately this led to them missing lesions, especially if they were small or flat (cancer in situ).

The addition of Hexvix/Cysview was shown by Photocure in its clinical trial programme to detect tumours that white light misses (see Exhibit 2). In total, 16% of patients had Ta (non-invasive papillary carcinoma) or T1 (cancer that invades from the surface epithelial layer into the connective tissue) tumours that were missed by the white light standard of care and were only detected through the use of Hexvix/Cysview. This is quite meaningful as bladder cancer is one of those cancers where there is a big difference between five-year survival rates for cancers that are caught early and those that are caught late. According to the National Cancer Institute, the five-year survival rate for those with localised cancer is 69.9%, 34% for those with regional and 5.4% for those where the cancer has distant metastases.

Exhibit 2: Phase III Hexvix/Cysview data

Patients	Hexvix/Cysview treatment group (n=365)
With ≥1 valid pathology result	365 (100%)
With ≥1 confirmed Ta or T1 tumour	286 (78%)
With ≥1 confirmed Ta or T1 tumour detected only by blue light	47 (16%)
p-value	0.001

Source: FDA

By improving tumour visibility, Hexvix/Cysview enables more complete removal of tumours, which then leads to longer recurrence-free survival, as studies have consistently shown across most subgroups (see Exhibit 3).

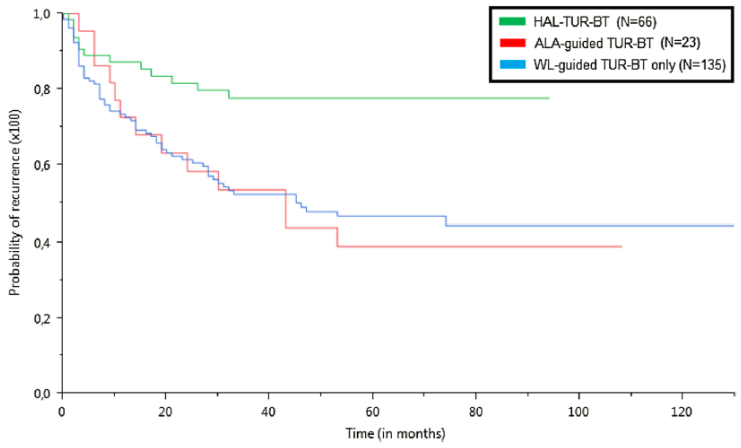
Exhibit 3: Hexvix/Cysview recurrence rate data

	Recurrence rate for patients where blue light was used, n (%)	Recurrence rate for patients where white light was used, n (%)	Total	Follow-up period	p-value
Hermann et al.	27/68 (39.7)	38/77 (49.4)	145	12 months	0.02
Stenzl et al	72/200 (36.0)	92/202 (45.5)	402	9 months	0.026
Dragoescu et al	8/42 (19.0)	17/45 (37.8)	87	12 months	0.0461
Total	107/310 (34.5)	147/324 (45.4)	634		0.006
At least one T1 or CIS	26/74 (35.1)	45/87 (51.7)	161		0.052
At least one Ta	92/256 (35.9)	119/268 (44.4)	524		0.04
High-risk subgroup	46/126 36.5)	70/144 (48.6)	270		0.05
Intermediate-risk subgroup	43/95 (45.3)	40/74 (54.1)	169		0.246
Low-risk subgroup	14/78 (17.9)	34/98 (34.7)	176		0.029

Source: European Association of Urology

Importantly, based on long-term data from a study by Georgios Gakis at the Department of Urology at Eberhard-Karls University in Tuebingen, Germany, the recurrence-free survival benefit is durable (see Exhibit 4, Hexvix/Cysview is the green line) with a p-value of 0.002 in a 224-person trial.

Exhibit 4: Recurrence-free survival Kaplan-Meier curves



Source: World Journal of Urology

Hexvix/Cysview's performance on the market

Photocure is commercialising Hexvix/Cysview in the US and the Nordics and is using partner Ipsen to market Hexvix in the rest of the EU. Also, new partnership deals were recently signed, which will allow Hexvix/Cysview to be available in Australia/New Zealand (Juno Pharma) and Canada (Biosyent). It has been successful in the Nordic region, where it has been able to achieve 39% market share as the therapy is not linked to a specific device, reimbursement is favourable and the company is based in Norway. Unfortunately, with only around 26 million people in the entire Nordic area, even this sizeable market share does not lead to meaningful sales (currently at a NOK40m annual run rate as of Q215, which is slightly less than $5m at current exchange rates). Also, while it was able to grow Nordic sales 19% in the second quarter compared to last year, only 6% of that was due to unit sales, the rest was due to timing of supply to distributors and price increases.

The big growth market into which Photocure is selling is the US, where revenue increased by 118% year-on-year in Q215. Unit sales increased 55%, with the rest coming from price increases and a strong dollar. Q215 sales were at a NOK23.2m (~$3m) annual run rate. Sales remain low despite a launch in 2012 because of the company's limited sales and marketing infrastructure, as well as unfavourable reimbursement. The company has approximately 15 sales and marketing representatives in the US, which has allowed it to penetrate and service 58 hospitals and urology

centres (up from 51 at the end of 2014 and 47 at the end of Q214). Additionally, the FDA requirement that the product is used in conjunction with the Karl Storz Photodynamic Diagnostic D-Light C System has been a further impediment to hospital penetration, as a capital purchase by the hospitals will likely be necessary. The cost of the device is $100-120k, which is around $20k more expensive than the standard white light-only device. Ultimately, the company would like to target the top 400 centres, which represent around 80% of TURB procedures.

Another issue is that Medicare does not separately reimburse centres for use of the Hexvix/Cysview blue light procedure, but instead bundles it with the total reimbursement for TURB, which is estimated at around $2,000.[1] This means that the ~$800 cost of the product comes out of the centre's profits and therefore there is no financial incentive for its use. Also, as the imaging solution takes one hour to be absorbed by the bladder, it increases the time of the entire procedure, further hurting profits. As bladder cancer is definitely a cancer of the elderly, with 72.1% over the age of 65 at the time of diagnosis (mean age is 73 years), Medicare is the key third-party payor. So, despite the fact that around 40% of private insurers reimburse for the procedure, it is not enough to move the needle meaningfully. Without profitability, procedures tend to be limited to use in academic/teaching centres, which are less concerned than community hospitals with profits.

Although a cost-effectiveness study indicated that the five-year overall costs of a patient who is given Hexvix/Cysview are lower than for a patient who initially only received white light ($25,921 vs $30,581[2]) due to lower downstream costs related to recurrence (see Exhibit 5), it is unlikely that Medicare reimbursement will change in the near term.

Exhibit 5: Medicare reimbursement for bladder cancer-related procedures

Procedure	Medicare payment (median)
TURB	$1,984.61
Radical cystectomy	$24,433.27
Partial cystectomy	$16,577.69
Chemotherapy	$6,000.00
Neoadjuvant chemotherapy	$6,000.00
Ongoing surveillance of muscle invasive disease	$18,638.88

Source: Canadian Journal of Urology

The company is attempting to go down the legislative route to get a separate reimbursement code for Hexvix/Cysview and there are two bills that have been introduced to achieve that end: HR 1178 and S 1466. The bills do not mention the product specifically, but rather make it so Medicare reimburses contrast agents separately in certain cases (this fact means we might see other companies with imaging agents starting to get involved on behalf of these bills).

Unfortunately, this process can have very extended timelines (from months to years) and can be expensive if lobbying is used. HR 1178 was introduced in the House of Representatives on 27 February 2015 and referred to the Subcommittee on Health on 6 March 2015, but has had no further action since. The Senate version was introduced on 22 May 2015 and referred to the Committee on Finance, again with no further action.

Besides increasing sales and marketing personnel and lobbying to change Medicare reimbursement, the company is also seeking a label expansion for Hexvix/Cysview, which could greatly increase its market potential. Currently, Hexvix/Cysview is used in of the initial diagnosis and treatment of patients as part of the TURB procedure. However, following TURB, patients will undergo surveillance in the form of cystoscopy examinations every three to nine months. So, while there are an estimated 250,000 TURB procedures in the US and another 300,000 in the EU, there are 1.2m surveillance procedures in the US and another 750,000 in the EU. Photocure has initiated

1 Garfield et al., Canadian Journal of Urology; 20(2); April 2013.

2 Ibid.

a 360 patient study to obtain this label expansion and is planning to commence recruitment of patients in H215 with results in 2017.

We currently model peak Hexvix/Cysview revenues to Photocure of NOK373m (~$45m) in 2020, which takes into account a label expansion in 2018 to include the surveillance market. We consider this to be very reasonable given that the TURB market alone has $400-500m in market potential, but we assume that the limited sales and marketing infrastructure and unattractive reimbursement in the US continues to hamper product adoption. While patents are set to expire in 2019 in the EU and 2020 in the US, we expect there to be a slower decline than usual when a drug goes generic due to the nature of Hexvix/Cysview as a drug/device combination. There is likely to be limited generic competition as generic companies are not specialised in devices. Also, as Hexvix/Cysview is part of a procedure rather than part of a pharmaceutical benefit for patients, payers are unlikely to force conversion to the generic product and hospitals will be able to make their own decisions, based largely on price and physician preference.

Cevira for HPV-related diseases

Cevira is a non-invasive photodynamic therapy based on a gel form of HAL under development for HPV-related (cervical) diseases and the company was recently granted an SPA for the registration programme in the US. To gain US approval, the company will need to run two randomized studies with 200 patients each, comparing Cevira to placebo in women with biopsy-verified, high-grade cervical lesions. The company is currently seeking partners to fund the development of Cevira, which should be easier now that it has an SPA in place.

Cervical cancer is caused by HPV, which can cause normal cells on the cervix to become abnormal. It can take five to 10 years after infection for cells to become abnormal, with abnormal cells graded either as low-grade squamous intraepithelial lesions (LSIL) or high-grade squamous intraepithelial lesions (HSIL). LSIL usually indicates mild dysplasia (normally graded as CIN1) with a 13% chance of turning into a more severe form of dysplasia (CIN 2/3) over the next two years, according to the American Academy of Family Physicians. Also, only about 2% progress to cervical cancer within 10 years, while 74% regress to normal in five years and 88% regress to normal in 10 years).[3] Due to this low risk of progression to cancer and high probability of regression to normal, LSIL is often untreated, with “watch and wait” being the dominant paradigm.

Patients with HSIL have around a 15-20%[4] chance of getting cervical cancer and so those patients are usually treated in a number of ways, either by ablative or excisional treatments (see Exhibit 6).

Exhibit 6: Abnormal cervical cell treatment comparison

Procedure	Description	Efficacy (%)	Positives	Negatives	Inpatient or outpatient	Procedure time
Laser ablation therapy	A beam of high-intensity light is used to eliminate abnormal cells.	95-96%	Efficacious.	Risk of bleeding, expensive equipment.	Outpatient	10-15 minutes
Cryotherapy	A probe is placed next to the cervix, cooling it to sub-zero temperatures and damaging the abnormal cells.	77-93%	Easy to perform, requires minimal equipment, associated with minimal discomfort, relatively fast.	Does not necessarily kill cells near periphery of probe or cells deep in the tissue, reducing efficacy.	Outpatient	10 minutes
Loop electrosurgical excision procedure (LEEP)	An electrified fine wire loop is used to remove abnormal tissue.	91-98%	Quick, efficacious and safe procedure with rare complications.	Higher risk of premature labour, requires expensive equipment.	Outpatient	10-20 minutes
"Cold knife" or laser conisation	A cone or cylinder-shaped piece of the cervix is removed with a laser or by cutting with a scalpel.	90-96%	Efficacious.	Often requires general anesthesia, bleeding risk.	Inpatient	Several hours (including recovery room time)

Source: The Cochrane Collaboration, WebMD

3 Holowaty et al. Journal of the National Cancer Institute, Vol. 91, No.3 February 3, 1999.
4 Cervical Cancer by Ruth Dunleavey.

Cevira treatment consists of an HAL gel, along with a disposable battery-powered LED device that is inserted next to the cervix. The HAL gel surrounds the service and after five hours, the time it takes for the gel to enter infected cells and be metabolised, the device's LEDs are activated for 4.5 hours. The LEDs then activate the drug and kill the abnormal, precancerous cells (although some normal cells are also killed).

The company ran a 262-patient Phase IIb trial comparing three different concentrations of HAL gel (0.2%, 1% and 5%) to placebo. The primary endpoint was lesion response rate at three months, with a response originally defined as histological regression to CIN1 or normal, cytology of LSIL or less severe and HPV negative. The 0.2% and 1% doses were no different from placebo, although the 5% dose showed a 73% response in confirmed CIN1/2 patients vs 60% placebo (p=0.2). However, there was a statistically significant response in the HAL 5% dose patients with confirmed CIN2. 18/19 (95%) of patients in the HAL arm compared to 12/21 (57%) patients in placebo responded (p<0.001). Importantly, among patients with the oncogenic HPV 16/18 subtypes, which are responsible for 70%[5] of cervical cancer cases, HPV clearance was seen in 5/6 (83%) patients in the HAL arm compared to 2/6 (33%) in placebo at the six-month point.

Importantly, at the behest of the FDA, the company conducted a reanalysis of the results, which included a new pathological assessment conducted by a panel of three independent pathologists (originally the samples were only read by one pathologist) and applied new clinical success criteria. As a result of this re-read of the results, 76% of HSIL patients in the Cevira group responded compared to 28% in the treatment arm, a statistically significant difference. These new success criteria are the same as will be used in the company's Phase III trial, and the trial itself is powered to succeed even if the treatment difference is half that seen in the Phase IIb.

Of course, a major caveat here is that the previous data are from small numbers of patients. Out of a 262-patient trial, these data come from less than 20% of the total intent-to-treat trial population. As a result, and the fact that there is additional partnership risk (Cevira will not move forward without one), we are attributing a 50% probability of success, which is less than the 60-70% probability typical of Phase III programmes.

In terms of pricing, most of the competitive technologies have relatively low reimbursement (see Exhibit 7), although there is high variability between payers and between procedures. Also, based on a cost-effectiveness study comparing Cevira treatment to excisional conisation procedures, the authors calculated that the risk of premature birth added approximately $630 per treatment.[6] The company could therefore argue that $1,000 per treatment is fair given the price savings long term from fewer premature deliveries.

Exhibit 7: Reimbursement rates for abnormal cervical cell therapies

Payor	Cryosurgery	Laser ablation	LEEP
Medicare (2014)	$149.38	$148.66	$288.73
BCBS-PPO (2012)	$300.58	$205.81	$242.93
Aetna (2012)	$198.94	$160.34	$402.64
United Health (2012)	$167.17	$136.61	$315.46
Cigna (2012)	$170.72	$76.90	$343.70

Source: CryoPen

Treatment of abnormal cervical cells related to HPV is still a large market. There are 50m pap tests performed each year in the US alone, with approximately 5% returning an abnormal test result. Most of these cases are LSIL, with the number of HSIL cases around 500,000 in the US according to the American College of Pathology, with a similar amount in Europe, making the addressable market around one million. Our model assumes a signed partnership next year with upfront and milestone payments with a 17.5% royalty and peak penetration of 17% of the HSIL cases treated with Cevira. Sales peak in 2030 at NOK2.4bn (~$290m) and then fall following the expiration of the

5 Bosch et al.,International Journal of Gynecology and Obstetrics (2006) 94 (Supplement 1), S8-S21.
6 Soergel et al. Lasers in Surgical and Medicine, 2011 Sep;43(7):713-20.

method-of-use patent, although we assume there will be residual sales for the same reasons as those for Hexvix/Cysview and the fact that the light device will have residual patents through 2034. We do not currently include any life cycle management opportunities with regard to Cevira in our model.

Visonac: Clearing things up

Visonac is a photodynamic therapy for moderate to severe inflammatory acne. It is a cream that contains methyl aminolevulinate (MAL) as its active ingredient, which is the same active ingredient as that of Metvix, Photocure's first approved product for skin cancers and was divested to Galderma in 2009 for €51m. It works by killing the bacteria *P. acnes* and decreasing sebum (oil) production.

Acne is a very common skin condition that has near-universal prevalence during teenage years. Approximately 95-100% of boys and 83-85% of girls aged 16-17 years old are affected by the condition, with 10-20% having the moderate to severe form.[7] In total, there are an estimated 40-50 million Americans of all age groups that suffer from the condition.[8] Approximately half of those are between the ages of 15-24 and, if 10-20% have moderate to severe acne, it would mean a prevalence of around 2-2.5 million moderate to severe patients.

There are quite a few types of treatment for Acne, which include over-the-counter medications (salicylic acid, benzoyl peroxide and vitamin A) and prescription medications (topical or oral antibiotics and hormonal therapy for women). Treatments generally work by reducing oil production, unblocking pores and/or killing acne-causing bacteria. More severe forms of acne are often treated with Accutane (isotretinoin) or oral antibiotics such as Solodyn (minocycline). Unfortunately, neither is 100% effective, with approximately 50% of patients failing treatment according to a market research study conducted by the company. On the safety side, Accutane in particular is considered to be rather toxic, and is associated with birth defects and liver abnormalities.

Visonac therapy consists of applying the cream to the face and allowing it to be absorbed by the skin and bacteria in the pustules for 90 minutes. The cream is then washed off and the face is exposed to red light for 10 minutes. This process is then repeated an additional three times over the next six weeks. In a 153-patient Phase IIb trial, Visonac demonstrated efficacy that was comparable to and possibly slightly better than Solodyn, which in 2011 had $761m in sales in the US (see Exhibit 8). There were no serious adverse events, but 12% of those in the treatment arm (compared to 0% in the placebo arm) dropped out of the trial due to adverse events, mainly burning/pain during illumination, which was an issue seen with Metvix and other MAL studies over the years.

Exhibit 8: Visonac vs Solodyn

Drug	Treatment arm: % change in inflammatory lesion counts from baseline at week 12	Placebo arm: % change in inflammatory lesion counts from baseline at week 12	Placebo-adjusted % change in lesion counts	p-value	Drop-out rate due to adverse events (%)
Solodyn (Study 04, n=451)	43.1	31.7	11.4	p=0.001	3.0
Solodyn (Study 05, n=473)	45.8	30.8	15.0	p<0.001	2.5
Visonac (Phase IIb, n=153)	43.8	26.6	17.2	p=0.003	12.0

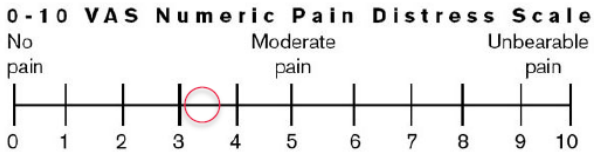
Source: FDA, clinicaltrials.gov

In terms of pain severity, the mean score on the visual analogue scale (0-10) was 3.38 (range 0-8.8) compared to 0.52 (range 0-3.6) for placebo. This indicates a mild to moderate amount of pain on average for most patients (see Exhibit 9). Also, 86% of patients in the treatment arm had mild to moderate and 3% severe facial reddening (resolved by day two) compared to 70% with mild to moderate reddening in the treatment arm.

7 Burton et al., British Journal of Dermatology, 1971 Aug;85(2) 119-26.

8 Zeichner et al., Journal of Drugs in Dermatology 2013 Dec;12(12):1416-27.

Exhibit 9: Visual analogue scale (VAS) for pain



Source: Photocure

In terms of the future of Visonac, the company is currently seeking a partner to further the development of the product. Like Cevira, there is an SPA associated with the product, lessening regulatory uncertainty (although it was already lower-risk given that it has the same active ingredient as Metvix, which was approved globally). However, despite the fact that the Phase IIb data have been available since May 2012 and the SPA was granted in 2013, no partnership agreement has been signed to date.

Our model currently assumes a 60% probability of success for the programme. It would be higher given the data and the regulatory history of MAL, but the extended period without a partner prompts us to lower it. We would otherwise give it a 70-80% chance of success. We also assume the company will sign a partnership in 2016, with upfront and milestone payments and a 17.5% royalty rate, with approval in 2020. We expect the price per treatment to be NOK2,500 or $300, comparable to other therapies for acne. Peak sales should hit NOK2.2bn (~$260m) in 2029, which is around one-third of Solodyn's peak sales. As this is a drug/device combination product like Hexvix/Cysview and Cevira, we also expect sales to continue past the expiration of its method-of-use patent in 2029, at least until the expiration of the full-face lamp patent in 2033.

Sensitivities

Photocure is subject to various sensitivities common to pharmaceutical product companies, including development, commercialisation, competitive, reimbursement and patent expiration risks. Hexvix/Cysview is growing very well in the US and could potentially have a surge in sales following approval for the surveillance market, expected around 2018, but the patent runway is short. Patent protection expires in the EU in September 2019 and in the US in November 2020 (however, we assume there are residual sales due to the drug/device combination nature of Hexvix/Cysview). Also, the current major impediments to Hexvix/Cysview adoption in the US are not likely to be resolved any time soon, namely poor reimbursement (eg for Medicare patients, the cost of Hexvix/Cysview comes directly from the hospital's bottom line as it is not reimbursed separately), as well as too few sales and marketing resources behind the product. The company is attempting to resolve the reimbursement issue through legislation, but that is a long and potentially expensive process that could last past patent protection.

With regard to Cevira, although it has just had an SPA approved by the FDA, it is a high-risk programme as its proof of efficacy comes from a subgroup of a subgroup representing only ~20% of the patients within a larger trial. Also, there are competitive excisional and ablative procedures, often with 90%+ efficacy, which are quick and relatively inexpensive. Cevira does have the advantage over the excisional procedures of little premature labour risk, but that is less of an argument against the ablative procedures. Finally, the company has said it needs to find a partner to fund the Phase III programme, so it could be on hold for quite some time.

For Visonac, while data have been promising and it also has an SPA with the FDA, it has been Phase III-ready since 2013 as the company has sought a partner, which leads one to question whether potential partners agree on its market potential due to the fact that it requires four visits to a physician's office for close to two hours each over the course of six weeks. It is a treatment

regimen that is simply not as convenient as oral antibiotics and creams, which are typically prescribed for acne.

Valuation

Using a risk-adjusted NPV model with a 10% discount rate for Hexvix/Cysview and 12.5% for Cevira and Visonac, we arrive at a value for Photocure of NOK1,523m or NOK71 per basic share (NOK67 per diluted share). As the company has indicated that it is seeking partners to continue the development of both Cevira and Visonac, we have assumed that it will receive a 17.5% royalty rate, as well as milestones for both products. For Cevira, we assume NOK80m (~$10m) upfront and an additional NOK160m (~$20m) in milestones, as well as a 17.5% royalty. For Visonac, we assume NOK80m (~$10m) upfront and an additional NOK280m (~$33m) in milestones, as well as a 17.5% royalty. Also, as Photocure's products are drug/device combinations, we assume that sales do not completely evaporate on patent expiration, as not all generic companies have the skills necessary to develop a drug/device combination. Also, as all its products are physician administered in the office/hospital setting, physicians will have more of a say as to whether to stay with the branded product, especially in the case of bundled (eg bladder cancer diagnosis) or typically non-reimbursed (eg acne) procedures.

Exhibit 10: Photocure valuation

Product	Main indication	Status	Probability of commercialisation	Launch year	Peak sales (NOKm)	Patent protection	Economics	rNPV
Hexvix/Cysview	Bladder cancer detection	Market	100%	Launched	NOK 373	2019-2020	Fully owned - US and Nordics, Partner with Ipsen in EU (35% royalty)	NOK664
Cevira	HPV-related diseases	Phase III	50%	2020	NOK 2,399	2030	17.5%	NOK333
Visonac	Acne	Phase III	60%	2020	NOK 2,175	2028	17.5%	NOK379
Total								NOK1,376
Cash and cash equivalents (Q215) (NOKm)								NOK147
Total firm value (NOKm)								NOK1,523
Total basic shares (m)								21.4
Value per basic share (NOK)								NOK71
Options (Q2/2015, m)								1.4
Total number of shares								22.8
Diluted value per share ($)								NOK67

Source: Edison Investment Research

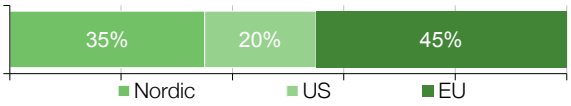
Financials

The Hexvix/Cysview franchise is profitable, with NOK14.1m in operating profits through Q215, compared to NOK8.7m in the previous year. US revenue is the main growth driver, as it is up 117% so far this year compared to last year. We expect mid-teens annual revenue growth over the next two years, with operating profit achieved in 2017. With NOK146.7m in cash and the possibility for upfront and regulatory milestone payments, Photocure should have enough capital to meet its needs. However, that will partially depend on the level of upfront and milestone payments, as well as royalties from potential partners.

Exhibit 11: Financial summary

NOK'000s	2012	2013	2014	2015e	2016e	2017e
Year end 31 December	IFRS	IFRS	IFRS	IFRS	IFRS	IFRS
PROFIT & LOSS						
Revenue	133,823	83,616	128,952	129,727	151,643	170,396
Cost of Sales	(9,405)	0	(6,996)	(8,753)	(10,615)	(11,928)
Gross Profit	124,418	83,616	121,956	120,975	141,028	158,469
Sales, General and Administrative Expenses	(113,583)	(114,657)	(95,032)	(109,918)	(114,315)	(118,888)
Research and Development Expense	(50,083)	(33,976)	(32,554)	(31,705)	(32,973)	(34,292)
EBITDA	(39,248)	(71,846)	(5,630)	(20,648)	(6,260)	5,289
Operating Profit (before GW and except.)	(39,248)	(71,846)	(5,630)	(20,648)	(6,260)	5,289
Intangible Amortisation	0	0	0	0	0	0
Other	0	0	0	0	0	0
Exceptionals	0	(3,694)	0	0	0	0
Operating Profit	(39,248)	(75,540)	(5,630)	(20,648)	(6,260)	5,289
Net Interest	8,236	8,688	7,157	4,259	4,430	4,607
Other	(11,356)	(14,015)	(15,573)	(14,544)	(15,126)	(15,731)
Profit Before Tax (norm)	(31,012)	(63,158)	1,527	(16,389)	(1,830)	9,896
Profit Before Tax (FRS 3)	(42,368)	(80,867)	(14,046)	(30,933)	(16,956)	(5,835)
Tax	890	8,204	(0)	0	0	0
Deferred tax	0	0	(0)	(0)	(0)	(0)
Profit After Tax (norm)	(30,122)	(54,954)	1,527	(16,389)	(1,830)	9,896
Profit After Tax (FRS 3)	(41,478)	(72,663)	(14,046)	(30,933)	(16,956)	(5,835)
Average Number of Shares Outstanding (m)	21.3	21.2	21.3	21.5	21.7	22.0
EPS - normalised (NOK)	(1.42)	(2.59)	0.07	(0.76)	(0.08)	0.45
EPS - FRS 3 (NOK)	(2.79)	(3.44)	(0.66)	(1.44)	(0.78)	(0.27)
Dividend per share (NOK)	0.0	0.0	0.0	0.0	0.0	0.0
BALANCE SHEET						
Fixed Assets	104,902	104,759	76,512	70,087	69,231	69,313
Intangible Assets	59,951	51,969	42,393	42,856	42,856	42,856
Tangible Assets	4,111	3,681	3,056	2,900	2,044	2,126
Other	40,840	49,109	31,063	24,331	24,331	24,331
Current Assets	328,076	197,020	194,067	167,428	159,220	177,096
Stocks	9,826	12,624	13,237	12,480	12,979	13,498
Debtors	15,432	17,085	15,585	23,102	24,026	24,987
Cash	302,818	167,258	165,245	131,846	122,214	138,610
Other	0	53	0	0	0	0
Current Liabilities	(51,089)	(30,307)	(27,466)	(25,099)	(25,099)	(25,099)
Creditors	(51,089)	(30,307)	(27,466)	(25,099)	(25,099)	(25,099)
Short term borrowings	0	0	0	0	0	0
Long Term Liabilities	(1,621)	(2,296)	(3,055)	(3,468)	(3,468)	(3,468)
Long term borrowings	0	0	0	0	0	0
Other long term liabilities	(1,621)	(2,296)	(3,055)	(3,468)	(3,468)	(3,468)
Net Assets	380,268	269,176	240,058	208,948	199,883	217,842
CASH FLOW						
Operating Cash Flow	(54,927)	(99,722)	(6,088)	(29,730)	(12,171)	13,755
Net Interest	0	0	0	0	0	0
Tax	0	0	0	0	0	0
Capex	0	0	(748)	(7,879)	(882)	(917)
Acquisitions/disposals	0	0	0	0	0	0
Financing	0	0	0	0	0	0
Dividends	0	0	0	0	0	0
Other	9,073	4,518	4,138	3,290	3,422	3,558
Net Cash Flow	(45,854)	(95,204)	(2,698)	(34,319)	(9,632)	16,396
Opening net debt/(cash)	(355,173)	(302,818)	(167,258)	(165,245)	(131,846)	(122,214)
HP finance leases initiated	0	0	0	0	0	0
Exchange rate movements	(1)	0	(1)	2	0	0
Other	-6500	-40356	686	918	0	0
Closing net debt/(cash)	(302,818)	(167,258)	(165,245)	(131,846)	(122,214)	(138,610)

Source: Company accounts, Edison Investment Research

Contact details	Revenue by geography
Photocure ASA Hossveien 4 0275 Oslo Norway +47 22 06 22 10 www.photocure.com	

Management team

President and CEO: Kjetil Hestdal

Kjetil Hestdal has served as president and CEO since January 2005. Dr Hestdal held the position as VP of Research and Development from January 1997 and was promoted to COO in October 2004. Before joining Photocure, he served as the project manager/medical expert at Sandoz (now Novartis) and as senior scientist at Rikshospitalet. He holds a PhD in immunology.

CFO: Erik Dahl

Erik Dahl joined Photocure in August 2012 as CFO. Most recently, he was CFO for GET AS, the second largest cable TV provider in Norway. He has more than 20 years' experience in senior level financial management roles, with responsibilities in corporate finance, legal and financial restructurings, M&A and capital market transactions. He has held various CFO roles in both public and private companies. Mr Dahl has a degree in finance and accounting from the Norwegian School of Economics.

COO: Kathleen Deardorff

Kathleen Deardorff joined the company in May 2011. She graduated from Purdue University School of Pharmacy, US with a PharmD. Kathleen has held senior leadership positions in strategic marketing, operational marketing and business development, crossing multiple geographies at Bristol-Myers Squibb and GE Healthcare. Her most recent position was head of global marketing at GE Healthcare, encompassing strategy development and global execution for both marketed and pipeline products for medical diagnostics portfolio.

Head of US Cancer Commercial Operations: Ambaw Bellette

Ambaw Bellete joined the company in 2012. He has more than 22 years' experience in the biopharmaceutical and medical device industry. He has held senior executive positions across multiple therapeutic areas in business development, commercial operations, managed care, marketing and sales at companies such as Pharmacia and Sanofi. He was most recently president of Medical Compression Systems.

Principal shareholders	(%)
JP Morgan Chase	14.72
Radiumhospitalets Forskningsstiftelse	9.00
Fonfdsfinans Norge	7.00
KLP Aksje Norge VPF	5.97
Kommunal Landspensjonskasse	4.43
MP Pensjon PK	3.85
Skagen Vekst	2.92

Companies named in this report

The Medicines Company (MDCO)