EDISON

Photocure

Company outlook

The stars are aligning for fast growth in the US

Pharma & biotech

Photocure is a commercial-stage Norwegian specialty pharmaceutical company that currently markets Hexvix/Cysview for diagnosing and managing bladder cancer. Recently, the company announced that the US Centers for Medicare & Medicaid Services (CMS) issued a final rule that would improve reimbursement for a large number of procedures. Also, following positive Phase III results in the surveillance setting, the company filed a supplemental New Drug Application (sNDA) which, if approved, would dramatically increase the addressable market for Hexvix/Cysview.

Year end	Revenue (NOKm)	PBT* (NOKm)	EPS* (NOK)	DPS (NOK)	P/E (x)	Yield (%)
12/15	134.7	(17.4)	(0.82)	0.0	N/A	N/A
12/16	143.6	12.8	0.59	0.0	45.4	N/A
12/17e	150.0	(43.9)	(2.04)	0.0	N/A	N/A
12/18e	242.5	10.2	0.47	0.0	57.0	N/A

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

Major reimbursement change in the US

The CMS has issued a final rule, which is set to take effect at the beginning of 2018. The rule significantly improves the reimbursement (by ~$1,000) for certain blue light cystoscopy (BLC) with Hexvix/Cysview procedures in Medicare patients. As 73.4% of bladder cancer patients are over 65, according to the National Cancer Institute, this should help accelerate penetration of the product in the US.

Surveillance trial data potentially transformational

Data from the 304-patient Phase III trial of Hexvix/Cysview in the surveillance setting showed that the product increased detection of patients with recurrence and that 21.5% ($p<0.0001$) of the patients with recurrence had one that was only detected with Hexvix/Cysview. Hexvix/Cysview sales may have significant upside if the product successfully expands into the US bladder cancer surveillance market, which has 1.4m procedures per year, compared to its current market of 300,000 transurethral resection of the bladder (TURB) procedures.

Assessing alternatives for Visonac and Cevira

In April, Photocure announced that after seeking partners for Cevira and Visonac (both Phase III ready) for the last few years, it is expanding the search to include outright sale of those products, possible spin-offs or other strategic alternatives. A spin-off in which a subsidiary is capitalised and then shares sold to outside investors appears the likely scenario for both products.

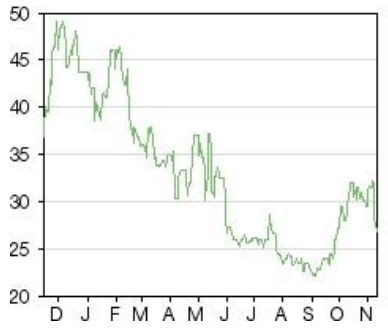
Valuation: NOK908m or NOK42 per share

We have adjusted our valuation to NOK908m or NOK42 per basic share from NOK949m or NOK44 per basic share, mainly due to pushing back expected launch dates for Cevira and Visonac from 2020 to 2021 as well as a lower cash balance, which was mitigated by rolling forward our NPV model to Q317. With NOK123.1m in cash, Photocure should have enough capital to meet its needs.

13 November 2017

Price	**NOK26.80**
Market cap	**NOK578m**
	NOK8.16/US$
Net cash (NOKm) at 30 September 2017	123
Shares in issue	21.6m
Free float	74.2%
Code	PHO
Primary exchange	Oslo
Secondary exchange	N/A

Share price performance



%	1m	3m	12m
Abs	(9.5)	11.7	(29.5)
Rel (local)	(11.0)	1.7	(42.2)
52-week high/low	NOK49.00		NOK22.10

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

CMS reimbursement change	1 January 2018
Surveillance market sNDA approval	H118

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Investment summary

Company description: Growing the franchise

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 has also developed Cevira and Visonac. Cevira 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 have over one million cases diagnosed annually in the US and EU and indicate a higher risk of cancer. Visonac is its 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. Both are Phase III ready.

Valuation: NOK42 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 NOK908m (from NOK949m), or NOK42 per basic share. Given the delay in securing partners for Cevira and Visonac and following the announcement in April regarding potential sale or spin-off, we have pushed back the expected launch of these products from 2020 to 2021, which also results in slightly lower peak sales estimates for both products.

Financials: Investing in the US market

The Hexvix/Cysview franchise has historically been profitable with NOK9.4m in EBITDA through the first three quarters of 2017, although this is down from NOK19.3m in the same period in 2016, mainly due to higher sales and marketing expenses in the US as the company prepares for a more intense marketing effort to coincide with the surveillance market launch. US revenue is the main growth driver as it is up 44% so far this year compared to last year. With NOK123.1m in cash, Photocure should have enough capital to meet its needs prior to profitability.

Sensitivities: Patent, development and regulatory risk

Photocure is subject to various sensitivities common to pharmaceutical product companies, including development, commercialisation, competition, reimbursement and patent expiration risks. Hexvix/Cysview should have a surge in sales following approval for the surveillance market, expected in H118, as well as the upcoming improvement in reimbursement, 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). 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. For Visonac, partners have had issues with the fact that the Phase IIb exclusively used the Nedax full-face lamp. If the Phase III used the same lamp and the product was approved on those data, it would require dermatologists to acquire another light source to use Visonac and many dermatologists already have multiple light sources in their office. A new partner might have to run additional Phase II trials with additional light sources to increase the chance of having a broader label and enabling dermatologists to use Visonac without additional capital expenditures.

A photodynamic therapy company

Photocure is currently focused on the development and commercialisation 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	Approval in the surveillance market in the US H118	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	Strategic options being assessed	Lower pre-term labour risk than surgical procedures
Visonac	Methyl aminolevulinate (MAL)	Moderate-to-severe inflammatory acne	Phase III	Strategic options being assessed	Potential efficacy in refractory patients

Source: Photocure

Hexvix/Cysview for the detection of bladder cancer

Hexvix/Cysview is a marketed colourless contrast solution, hexaminolevulinate hydrochloride (HAL), currently 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 on tumour detection

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: Burger M, et al. Photodynamic Diagnosis of Non–muscle-invasive Bladder Cancer with Hexaminolevulinate Cystoscopy: A Meta-analysis of Detection and Recurrence Based on Raw Data. Eur Urol (2013)

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 (three-year, recurrence-free survival was 77.8% for those patients where Hexvix/Cysview was used and 52.4% when white light was used) with a p-value of 0.002 in a 224-person trial.[1]

Phase III surveillance market data

Photocure presented new clinical results of Hexvix/Cysview at the American Urological Association (AUA) meeting on 14 May 2017. The results are from the Phase III clinical study measuring the utility of Hexvix/Cysview for the ongoing surveillance of patients with non-muscle invasive bladder cancer (NMIBC). After diagnosis, patients with NMIBC typically undergo a TURB procedure, in which tumours are resected using a cystoscope. Hexvix/Cysview is already approved for use during TURB procedures to improve the identification of lesions for removal. These patients are then followed with routine surveillance for recurrence, which is high with NMIBC. The AUA recommends surveillance every three to six months for the first three years after diagnosis and yearly thereafter.

The clinical trial enrolled 304 patients at 17 institutions in the US. It only enrolled patients with a high probability of recurrence, as identified by having multiple tumours, a previous recurrence, and/or high-grade tumours in previous procedures. Patients on the study underwent both blue light and white light cystoscopy and the ability of the two techniques to identify recurrence events was compared. The primary endpoint of the trial was the number of patients with recurrences who were identified using Hexvix/Cysview who were missed with white light cystoscopy. In addition to the experimental portion of the trial, 68 patients were included for training purposes to acclimatise physicians to blue light cystoscopy (BLC).

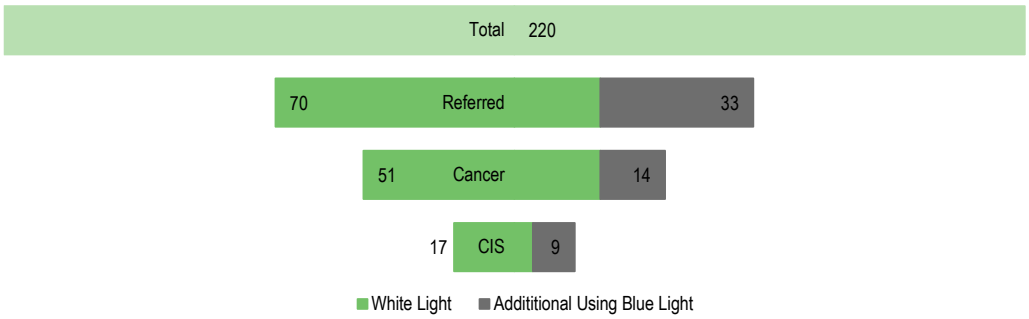
A total of 220 patients were in the experimental portion of the trial and available for evaluation. From this population, 103 patients were referred to the operating room for a TURB procedure based on initial surveillance cystoscopy, and 65 had a confirmed recurrence. 14 patients (21.5% $p<0.0001$) were referred to the operating room using Hexvix/Cysview and would have been missed using white light cystoscopy alone. This is significant evidence that Hexvix/Cysview can improve the surveillance in this population. Moreover, of these 65 patients with recurrence, almost half (30 patients, 46.2%) had additional lesions detected using Hexvix/Cysview over white light cystoscopy alone. In particular, Hexvix/Cysview improved the identification of carcinoma in situ (CIS). CIS is a small flat lesion in the early stages of its growth before it is generally considered a tumour with high risk of progression. Of the patients on the trial, 26 had confirmed CIS, of which nine (34.6%, $p<0.0001$) were diagnosed with Hexvix/Cysview and would have otherwise been missed.

1 Gakis et al., World Journal of Urology; (2015) 33:1429

The use of Hexvix/Cysview did substantially increase the number of false positive diagnoses of recurrence. It doubled the number of patients from 19 to 38 (8.6% to 17.2%) that were referred for TURB who turned out to not have a malignancy. The total number of patients referred for TURB increased by 47% (from 70 to 103) when using Hexvix/Cysview; however, we consider this increase in procedures justified considering that 42% of the new referrals had disease that would have otherwise been missed.

We believe that these data are supportive of approval for the US surveillance market. In addition, the safety data on repeated use of Hexvix/Cysview, as well as significantly improved detection of CIS obtained in the current study, should expand the current label to include improved detection of CIS and remove the current label restrictions on repeated use.

Exhibit 4: Blue light cystoscopy with Hexvix/Cysview increases bladder cancer detection



Source: Photocure

Expansion into the surveillance market is essential to the continued growth of Hexvix/Cysview, particularly in the US. The US bladder cancer surveillance market has 1.4m procedures per year, much larger than the currently approved market for Hexvix/Cysview, 300,000 transurethral resection of the bladder tumour (TURBT) procedures. The supplemental NDA was filed in August. In October, the FDA accepted it for review and granted priority review status, with a final decision expected in H118.

Hexvix/Cysview's performance on the market

Photocure is commercialising Hexvix/Cysview in the US and the Nordics. It is using partners such as Ipsen in the EU outside of the Nordics, BioSyent in Canada and Juno in Australia/New Zealand to market elsewhere.

Exhibit 5: Q317 Hexvix/Cysview sales

	Revenue (NOKm)	Y-o-y	Q-o-q	Units	Y-o-y	Q-o-q
Hexvix sales Nordic	8,969	3%	-23%	2,096	6%	-12%
Cysview sales US	11,292	45%	3%	1,500	39%	9%
Total own sales	20,261	23%	-10%	3,596	17%	-4%
Partner sales	15,218	1%	1%	10,144	-1%	-8%
Total Hexvix/Cysview	35,478	12%	-6%	13,740	3%	-7%

Source: Photocure

Hexvix/Cysview has been successful in the Nordic region, where it has been able to achieve ~40% 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 NOK40.5m annual run rate as of Q317, which is slightly less than $5m at current exchange rates). Also, growth has slowed with Q317 revenues only 3% higher than last year as the market is relatively mature.

Ipsen, which sells into the much larger non-Nordic EU market, has been relatively successful in doing so with a unit run rate five times higher than that of Photocure in the Nordics. However, there have been some issues recently. Results were strongly affected by a loss of reimbursement in France so that now hospitals must bear the additional cost of the product. This move is somewhat perplexing as the new French National Guidelines for bladder cancer, which were introduced in November 2016, recommend the use of blue light cystoscopy for the first bladder resection in almost all patients. In addition, growth in the relatively new markets of Australia and Canada (partnered with Juno and BioSyent, respectively) was hampered by the delayed placement of scopes and reimbursement issues. Partner revenue was up 1% in Q317 and is down 1% ytd.

The growth market into which Photocure is selling is the US. Year-on-year revenue growth in Q317 was 45% for the quarter and 44% for 9M17. Sales are being driven by an increase in the number of permanent blue light cystoscopes installed (currently 96, up from 83 at the beginning of the year and 65 at the beginning of 2016) and by an increase in the usage per centre. The current annualised run rate in the US is NOK43.1m ($5.3m). Sales levels have been relatively low despite a launch in 2012 because of the company's historically limited sales and marketing infrastructure, as well as unfavourable reimbursement, both of which are in the process of being resolved. The company is doubling the number of sales and marketing representatives in the US from 15 to 30 and will benefit once new CMS reimbursement takes effect on 1 January 2018.

Prior to this rule taking effect, Medicare had not separately reimbursed centres for use of the BLC with Hexvix/Cysview procedure, but instead bundled it with the total reimbursement for TURBT procedures, so any additional cost related to the product was absorbed by the centre. This has had a direct impact on the availability of BLC with Hexvix/Cysview in the US.

The issue could be potentially resolved as of 1 January 2018 thanks to a new rule finalised by CMS that would create a new code for blue light cystoscopy, which would improve reimbursement for the procedure in most situations to a level where the cost of the product would be covered. Effectively, for CPT codes 52204, 52214 and 52224, if blue light cystoscopy is used, they would qualify for reassignment to the higher ambulatory payment classification (APC) of APC 5374 from APC 5373. The company believes this will result in a $1,000 increase in reimbursement for the CPT codes 52204, 52214 and 52224. Based on CMS procedure figures (see Exhibit 6), this would affect 54% of procedures.

Exhibit 6: CPT codes used with Hexvix/Cysview

CPT Code	Description	APC	Number of procedures (2015)	% of Total
52204	Biopsy of the bladder using an endoscope	5373	36,566	18.3%
52214	Destruction of tissue in the bladder, bladder canal (urethra) or surrounding glands using an endoscope	5373	21,950	11.0%
52224	Destruction of (less than 0.5 centimeters) growths of the bladder and bladder canal (urethra) using an endoscope	5373	49,492	24.8%
52234	Destruction and/or removal of (0.5 to 2.0 centimeters) small growths of the bladder using an endoscope	5374	31,586	15.8%
52235	Destruction and/or removal of (2.0 to 5.0 centimeters) medium growths of the bladder and bladder canal (urethra) using an endoscope	5374	36,026	18.0%
52240	Destruction and/or removal of large growths of the bladder using an endoscope	5374	24,340	12.2%
Total			199,960	100%

Source: CMS. Note: The procedure numbers only include those reimbursed by medicare and not by commercial payers.

As bladder cancer is definitely a cancer of the elderly, with 73.4% over the age of 65 at the time of diagnosis (median age is 73 years) according to the National Cancer Institute, Medicare is the key third-party payer and this is a major win for the company.

Valuation assumptions

We currently model peak Hexvix/Cysview revenues to Photocure of NOK344m (~$42m) in 2020. Our current estimate takes into account a label expansion in H118 to include the surveillance market. We consider this to be very reasonable given that the TURB market alone has $400-500m

in market potential. 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 becomes 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 has an SPA in place with the FDA. To gain US approval, two randomised studies with 200 patients each, comparing Cevira to placebo in women with biopsy-verified, high-grade cervical lesions will be needed. The company is currently exploring strategic alternatives (including partnership, outright sale, spin-offs and other strategic alternatives) to further the development of Cevira, although no guidance on timing has been provided.

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 CIN 1) 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% of patients progress to cervical cancer within 10 years, while 74% regress to normal in five years and 88% regress to normal in 10 years.[2] 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%[3] 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 7).

Exhibit 7: 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 anaesthesia, bleeding risk.	Inpatient	Several hours (including recovery room time)

Source: The Cochrane Collaboration, WebMD

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 cervix 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).

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

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 CIN 1 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 CIN 1/2 patients vs 60% placebo (p=0.2). However, there was a statistically significant response in the HAL 5% dose patients with confirmed CIN 2. 18 of 19 (95%) patients in the HAL arm compared to 12 of 21 (57%) patients in placebo responded (p<0.001). Importantly, among patients with the oncogenic HPV 16/18 subtypes, which are responsible for 70%[4] of cervical cancer cases, HPV clearance was seen in five of six (83%) patients in the HAL arm compared to two of six (33%) in placebo at the six-month point.

Also, 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.

Of course, a major caveat here (and potentially a key reason why potential partners are hesitant) 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. Whoever takes over Cevira would either need to run another Phase II to better understand the risk-reward of a Phase III trial or simply stomach the risk with the understanding that they are moving forward with limited data.

In terms of pricing, most of the competitive technologies have relatively low reimbursement (see Exhibit 8), 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.[5] The company could therefore argue that $1,000 per treatment is fair given the price savings in the long term from fewer premature deliveries.

Exhibit 8: 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.

Valuation assumptions

Our valuation model assumes peak penetration of 16% of the HSIL cases treated with Cevira. Sales peak in 2030 at NOK2.2bn or around $270m (lower than our previous estimate of peak sales of NOK2.4bn because of a delay in the estimated launch year from 2020 to 2021 due to a lack of clarity on the path forward) and then fall following the expiration of the method-of-use patent. 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. We continue to assume only a

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

20% chance of success, much lower than the 60-70% we would normally assume for a Phase III asset due to the difficulty in finding a path forward for the asset.

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, which was divested to Galderma (now part of Nestlé) 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.[6] In total, there are an estimated 40-50 million Americans of all age groups that suffer from the condition.[7] Approximately half of those are between the ages of 15 and 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 (see Exhibit 9), which in 2011 had sales of $761m in the US. 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 9: 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. Also, 86% of patients in the treatment arm had mild to moderate and 3% had severe facial reddening (resolved by day two) compared to 70% with mild to moderate reddening in the control arm.

In terms of the future of Visonac, as with Cevira, the company is currently exploring strategic alternatives (including partnership, outright sale, spin-offs and other strategic alternatives) to further

6 Burton et al., British Journal of Dermatology, 1971 Aug; 85(2) 119-26.
7 Zeichner et al., Journal of Drugs in Dermatology 2013 Dec; 12(12):1416-27.

the development. Also like Cevira, there is an SPA associated with the product, reducing regulatory uncertainty.

Valuation assumptions

Our model currently assumes a 20% chance of success, which is much lower than we would normally use given the data and the regulatory history of MAL, but the extended period without a partner prompts us to use caution. We expect launch in 2021 (previously 2020) and peak sales of NOK2.1bn or around $260m (lower than our previous NOK2.2bn estimate due to uncertainty as to the path forward). 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, competition, reimbursement and patent expiration risks. Hexvix/Cysview should have a surge in sales following approval for the surveillance market, expected in H118, as well as the upcoming improvement in reimbursement, 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).

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. For Visonac, partners have had issues with the fact that the Phase IIb exclusively used the Nedax full-face lamp. If the Phase III used the same lamp and the product was approved on those data, it would require dermatologists to acquire another light source to use Visonac and many dermatologists already have multiple light sources in their office. A new partner might have to run additional Phase II trials with additional light sources to increase the chance of having a broader label and enabling dermatologists to use Visonac without additional capital expenditures.

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 valuation of NOK908m or NOK42 per basic share, down from our previous NOK949m or NOK44 per basic share. The reduction in the valuation is mainly due to pushing back expected launch dates for Cevira and Visonac from 2020 to 2021 on the back of the delays in advancing those products as strategic options continue to be explored. We have also slightly lowered our peak sales assumptions for these products as discussed above. The lower cash balance has also affected the valuation. That said, these changes were somewhat mitigated by rolling our NPV model forward to Q317.

Exhibit 10: Photocure valuation summary

Product	Main indication	Status	Probability of commercialisation	Launch year	Peak sales (NOKm)	Patent protection	Economics	rNPV (NOKm)
Hexvix/Cysview	Bladder cancer detection	Market	100%	Launched	344	2019-20	Fully owned - US and Nordics, Partner with Ipsen in EU (35% royalty)	564
Cevira	HPV-related diseases	Phase III	20%	2021	2,218	2030	17.5%	118
Visonac	Acne	Phase III	20%	2021	2,091	2028	17.5%	103
Total								784
Cash and cash equivalents (Q317)								123
Total firm value								908
Total basic shares (m)								21.6
Value per basic share (NOK)								42
Options (Q317, m)								0.0
Total number of shares (m)								21.6
Diluted value per share (NOK)								42

Source: Edison Investment Research

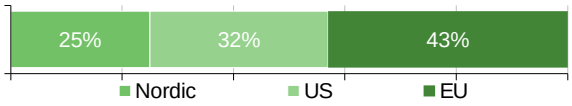
Financials

We are maintaining our estimates for the most part, although we have increased our 2017 sales estimate by NOK0.6m, increased our 2017 and 2018 R&D expense estimates by NOK0.6m and NOK0.7m, respectively and decreased our SG&A estimates by NOK6.1m in 2017 and NOK7.6m in 2018 due to a lower than expected run rate. We have also increased our estimates for capital expenditures for 2017 by NOK7.2m due to higher than expected spending on the recently completed surveillance study. We continue to expect that Photocure will become profitable in 2018, although we expect cash flows to be negative until 2019. The company ended Q317 with NOK123m in cash, and we do not expect it to require further financing.

Exhibit 11: Financial summary

NOK'000s	2015	2016	2017e	2018e
Year end 31 December	IFRS	IFRS	IFRS	IFRS
PROFIT & LOSS				
Revenue	134,717	143,627	149,998	242,457
Cost of Sales	(8,221)	(9,337)	(11,687)	(16,947)
Gross Profit	126,496	134,291	138,311	225,510
Sales, General and Administrative Expenses	(115,025)	(124,647)	(149,182)	(186,478)
Research and Development Expense	(29,558)	(17,652)	(22,202)	(23,090)
EBITDA	(18,087)	(8,008)	(33,073)	15,943
Operating Profit (before amort. and except)	(21,986)	(15,861)	(47,013)	6,943
Intangible Amortisation	0	0	0	0
Other	0	0	0	0
Exceptionals	0	0	0	0
Operating Profit	(21,986)	(15,861)	(47,013)	6,943
Net Interest	4,553	28,640	3,096	3,220
Other	(9,771)	(366)	(573)	0
Profit Before Tax (norm)	(17,434)	12,779	(43,917)	10,163
Profit Before Tax (FRS 3)	(27,205)	12,414	(44,490)	10,163
Tax	0	(0)	0	0
Deferred tax	(0)	(0)	(0)	(0)
Profit After Tax (norm)	(17,434)	12,779	(43,917)	10,163
Profit After Tax (FRS 3)	(27,205)	12,413	(44,490)	10,163
Average Number of Shares Outstanding (m)	21.4	21.5	21.6	21.8
EPS - normalised (ore)	(82)	59	(204)	47
EPS - FRS 3 (ore)	(127)	58	(206)	47
Dividend per share (ore)	0.0	0.0	0.0	0.0
BALANCE SHEET				
Fixed Assets	76,394	74,070	84,146	83,626
Intangible Assets	50,615	26,390	29,810	28,866
Tangible Assets	2,288	1,660	1,604	2,027
Other	23,490	46,020	52,732	52,732
Current Assets	171,670	212,268	160,172	169,940
Stocks	13,800	17,955	14,869	27,990
Debtors	23,844	12,323	16,040	24,246
Cash	134,026	169,239	112,784	101,225
Other	0	12,750	16,479	16,479
Current Liabilities	(34,039)	(30,637)	(24,308)	(24,308)
Creditors	(34,039)	(30,637)	(24,308)	(24,308)
Short term borrowings	0	0	0	0
Long Term Liabilities	(3,960)	(3,758)	(4,524)	(4,976)
Long term borrowings	0	0	0	0
Other long term liabilities	(3,960)	(3,758)	(4,524)	(4,976)
Net Assets	210,064	251,943	215,486	224,281
CASH FLOW				
Operating Cash Flow	(21,030)	19,193	(41,182)	(3,080)
Net Interest	0	0	0	0
Tax	0	0	0	0
Capex	(14,930)	(21,715)	(17,315)	(10,603)
Acquisitions/disposals	0	33,213	0	0
Financing	0	0	0	0
Dividends	0	0	0	0
Other	2,326	2,394	2,042	2,123
Net Cash Flow	(33,634)	33,085	(56,455)	(11,559)
Opening net debt/(cash)	(165,245)	(134,026)	(169,239)	(112,784)
HP finance leases initiated	0	0	0	0
Exchange rate movements	2	0	0	0
Other	2413	2129	0	0
Closing net debt/(cash)	(134,026)	(169,239)	(112,784)	(101,225)

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 of 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: Jeremy Bahr

Jeremy Bahr joined the company in 2017. He came from UCB, where his most recent role was global head of market analytics and where he previously served as head of commercial operations in North America. Prior to UCB, he spent seven years at Pfizer, where he held senior roles in marketing, sales and strategy. Earlier in his career he worked in private equity, as an entrepreneur and spent several years as a consultant at McKinsey & Company.

Head of US Cancer Commercial Operations: Ambaw Bellete

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	(%)
High Seas AS	11.80
Fondfinans Norge	6.10
KLP Aksje Norge VPF	5.62
Kommunal Landspensjonskasse	4.43
Radiumhospitalets Forskningsstiftelse	3.47
MP Pensjon PK	3.09
JP Morgan Chase Bank	3.01

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