EDISON

Photocure

Financial update

Rapid acceleration in the US market

Pharma & biotech

Photocure is a commercial-stage Norwegian specialty pharmaceutical company that currently markets Hexvix/Cysview for diagnosing and managing bladder cancer. The company recently announced Q418 results, including 27% revenue growth globally and 81% growth in the US, making it the largest and fastest growing region for the company. This growth has been driven by the approval and launch of Hexvix/Cysview in the surveillance setting and improved reimbursement.

Year end	Revenue (NOKm)	PBT* (NOKm)	EPS* (NOK)	DPS (NOK)	P/E (x)	Yield (%)
12/17	150.9	(41.6)	(1.61)	0.0	N/A	N/A
12/18	181.5	(22.5)	(1.04)	0.0	N/A	N/A
12/19e	240.1	19.5	0.65	0.0	71.5	N/A
12/20e	294.8	65.4	2.15	0.0	21.6	N/A

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

Phenomenal US growth

Q418 sales in the US increased 81% to NOK18.4m and are up 50% over the course of 2018 with a clear acceleration in the second half of the year. Unit sales increased 69% during the quarter and are up 45% for the year. The total installed base of blue light cystoscopes (both rigid and flexible) increased to 157, up 51% from 104 at the beginning of 2018.

Investing in US sales and marketing

As the company is looking to capitalise on the tailwinds of FDA approval for Hexvix/Cysview in the surveillance setting (which is triple the size of their original market) as well as improved Centers for Medicare and Medicaid Services (CMS) reimbursement, the number of customer-facing roles will increase by 50% in the US over the course of 2019 (mainly through repositioning current headcount), which will allow it to cover 75% of the metropolitan areas in the US.

Partner and Nordic sales growing

On a pro-forma basis (adjusting for IFRS changes), partner revenue increased 9% in the fourth quarter and 4% for the year, driven mainly by Germany and Canada. Nordic revenues were up 5% in Q418 and 9% for the year due to price increases.

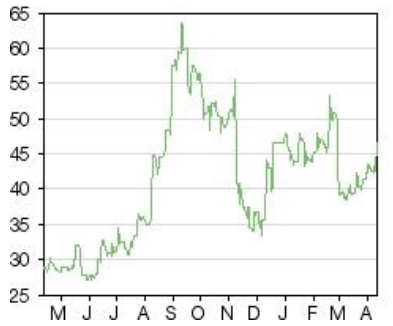
Valuation: NOK1,246m or NOK57 per share

We have increased our valuation to NOK1,246m or NOK57 per basic share, from NOK970m or NOK45 per basic share. We have increased our Hexvix/Cysview estimates as we believe there is less risk for competition for the product in the near to intermediate future. We have also eliminated Cevira and Visonac from the model as both products continue to be on hold as Photocure conducts a review of strategic options. Additionally, there was an increase in cash and NPVs were rolled forward. With NOK107m in cash, Photocure should have enough capital to meet its needs, as we expect profitability in 2019.

11 April 2019

Price	**NOK46.5**
Market cap	**NOK1014m**
	NOK8.55/US$
Net cash (NOKm) at 31 December 2018	107
Shares in issue	21.8m
Free float	73.0%
Code	PHO
Primary exchange	Oslo
Secondary exchange	N/A

Share price performance



%	1m	3m	12m
Abs	20.8	6.7	52.7
Rel (local)	18.8	3.0	49.8
52-week high/low	NOK63.50		NOK27.10

Business description

Photocure specialises in photodynamic therapy. Its bladder cancer imaging product is sold as Hexvix in Europe and Cysview in the US. It 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

Update on surveillance market launch	2019

Analysts

Maxim Jacobs	+1 646 653 7027
Briana Warschun	+1 646 653 7031

healthcare@edisongroup.com

Edison profile page

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 and Visonac is its treatment for inflammatory acne. Both are Phase III ready and the company is exploring strategic alternatives to continue their development.

Valuation: NOK57 per basic share

Using a risk-adjusted NPV model with a 10% discount rate for Hexvix/Cysview, we arrive at a value for Photocure of NOK1,246m (from NOK970m), or NOK57 per basic share. We have increased our Hexvix/Cysview estimates as we believe there is less risk for competition for the product in the near to intermediate future (we have moved our projected year of generic entry, and hence peak sales, to 2024 from 2020). Also, as the company has indicated it has filed additional patents (likely formulation patents) that could potentially protect the product until 2038, we have extended our model to include that year (previously our model ran to 2029). We have also eliminated Cevira and Visonac from the model as both products continue to be on hold as the company conducts a review of strategic options. Additionally, there was an increase in cash following the company achieving operating cash flow positive status during the quarter and NPVs were rolled forward.

Financials: Investing in the US market

The Hexvix/Cysview franchise has historically been profitable with NOK8.4m in EBITDA through 2018, although this is down from NOK10.4m in 2017, mainly due to higher sales and marketing expenses in the US as the company invests in a more intense marketing effort. US revenue is the main growth driver as it is up 81% in the fourth quarter and is up 50% for the year. With NOK107m in cash, Photocure should have enough capital to meet its needs prior to profitability, which we currently expect in 2019. Also, importantly, the company was operating cash flow positive in Q418, although this effect was partly seasonal due to working capital changes in the fourth quarter.

Sensitivities: Commercial and patent risk

Photocure is subject to various sensitivities common to healthcare product companies, including commercialisation, competition, reimbursement and patent expiration risks. Hexvix/Cysview is having a surge in sales following approval for the surveillance market, as well as an improvement in reimbursement, but its patent runway is short. Patents are set to expire in September 2019 in the EU and November 2020 in the US, although any potential competitor would likely need to run some sort of clinical trial and get approval from both the Center for Devices and Radiological Health and Center for Drug Evaluation and Research due to the nature of Hexvix/Cysview as a drug/device combination. This additional cost (both clinical and regulatory) would limit the attractiveness of this market to certain competitors, especially generic competitors, 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.

A commercial-stage healthcare company

Photocure is currently focused on the development and commercialisation of three products (see Exhibit 1), particularly on 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 high-grade squamous intraepithelial lesion (HSIL), which has more than one million cases diagnosed annually in the US and EU and indicates a higher risk of cancer. Visonac is a 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	Continued penetration in the newly approved surveillance market	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 tumour (TURBT) procedure as well as for patients undergoing a surveillance cystoscopy (a cystoscope is a thin tube with a lighted tip). The solution is administered into the bladder before cystoscopy. 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 conducted a 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 TURBT procedure, in which tumours are resected using a cystoscope. Hexvix/Cysview is already approved for use during TURBT 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.

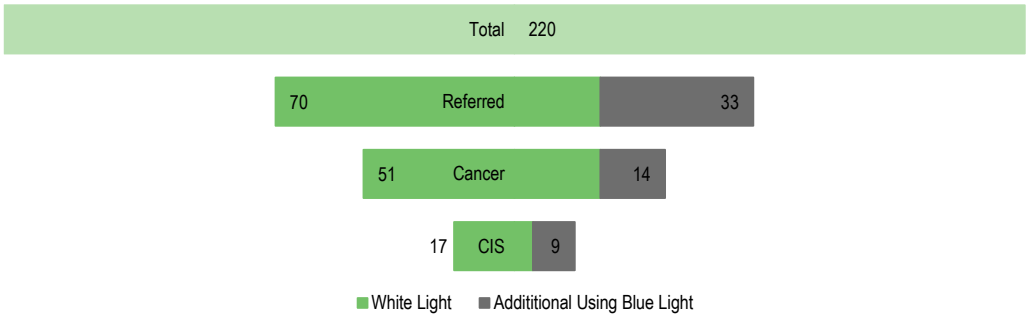
The clinical trial enrolled 304 patients at 17 institutions in the US. It only enrolled patients with a high probability of recurrence, as identified by having multiple tumours, a previous recurrence, and/or high-grade tumours in previous procedures. Patients on the study underwent both blue light and 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 TURBT 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

However, 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 TURBT who turned out to not have a malignancy. The total number of patients referred for TURBT 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.

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



Source: Photocure

In mid-February 2018, the company announced that the FDA had approved Hexvix/Cysview for use in the surveillance setting. Additionally, the current label has been expanded to include improved detection of carcinoma in situ (CIS) and all restrictions on repeated use have been removed. 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 original market for Hexvix/Cysview of 300,000 TURBT procedures.

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.

Hexvix/Cysview has been successful in the Nordic region, where it has been able to achieve between 25% and 70% market share (depending on the country) as the therapy is not linked to a specific device, reimbursement is favourable and the company is based in Norway and therefore Nordic in origin. Unfortunately, with only around 27 million people in the entire Nordic area, even this sizeable market share does not lead to meaningful sales (NOK47.0m, or about $5.5m, in 2018). Also, growth is now mainly driven by price increases. Full year revenues grew 9% but in-market unit sales over the same period fell by 4% (though this was mainly due to large deliveries to hospitals in Denmark close to the end of 2017).

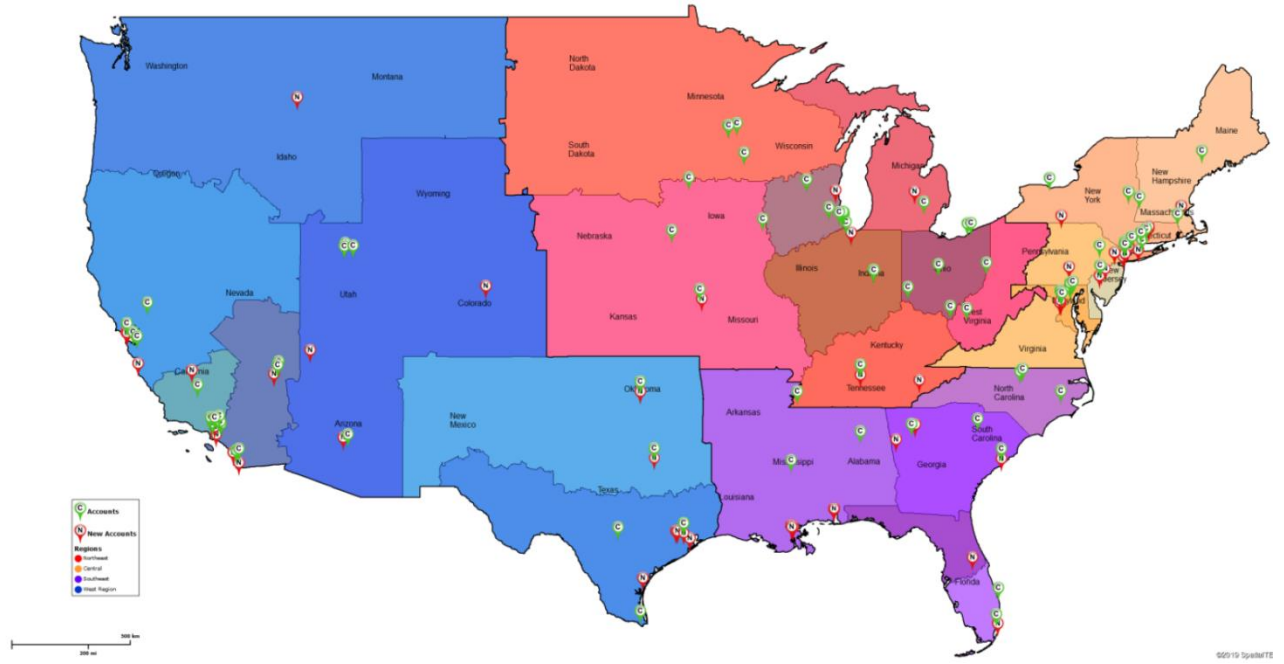
Ipsen, which sells into the much larger non-Nordic EU market, has been relatively successful in doing so, especially in Germany where it has a 30% penetration rate. However, there have been some issues that have had an impact on sales. Results were strongly affected by a loss of reimbursement in France 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. As a result, growth in unit sales in Germany was negated by a fall in volume in France so that total in-market unit sales for partner regions was flat. 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 though some revenues have begun to filter through from Canada. On a pro-forma basis (adjusting for IFRS changes) partner revenue increased 9% in the fourth quarter and 4% for the year. On a reported

basis (which uses a different accounting standard in 2017 and 2018), partner revenue was down 12% in Q4 and 2% for the year.

The US is Photocure's growth market. Year-on-year revenue growth in Q418 was 81% for the quarter and 50% for the full year. The current annualised run rate in the US is NOK73.6m ($8.6m). Sales are being driven by an increase in the number of permanent blue light cystoscopes installed (currently 157, up 51% from 104 at the beginning of 2018 and almost double the 83 that were installed at the beginning of 2017), which include eight flexible cystoscopes for use in the surveillance setting. These installations include 74% of National Comprehensive Cancer Network (NCCN) centres, 56% of National Cancer Institute (NCI) centres and almost three-quarters of the top 25 hospitals in the country (as ranked by US News and World Report).

While currently in a state of high growth, US sales had historically been challenging because of the company's historically limited sales and marketing infrastructure, as well as unfavourable reimbursement. Both issues are in the process of being resolved (or have been resolved). The number of customer-facing roles will increase by 50% in the US over the course of 2019 (from 21 to 31), which will allow them to cover 75% of the metropolitan areas in the US and over 750 accounts (up from 525 today). We believe this will mainly be achieved through repositioning current headcount.

Exhibit 5: Graphical representation of sales regions and account locations



Source: Photocure

Photocure has also been able to benefit from new CMS reimbursement rules, which took effect at the beginning of 2018 and 2019 (see Exhibit 6). The company estimates that with this most recent coding change, there will be coverage for Hexvix/Cysview for approximately all of the TURBT market in the United States, including both Medicare and private insurance. As a reminder, Medicare coverage is particularly important for Photocure as bladder cancer is 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, making CMS the key third-party payer.

Exhibit 6: US reimbursement summary for Hexvix/Cysview by setting

Procedure	Medicare	Private/commercial insurance
Cystoscopy	A procedure fee for the cystoscopy with Cysview paid at average selling price + 6% in clinic or physician's office setting with new code (A9589)	A procedure fee for the cystoscopy with Cysview paid at average selling price + 6–15% (depending on contract with private payer)
TURBT	Hospital outpatient departments will receive an additional $1,187 to cover the complexity of Cysview for codes 52204 and 52224. Reimbursement is bundled for codes 52214, 52234, 52235 and 52240 with a new add in code (A9589)	A procedure fee for the TURBT with Cysview paid at average selling price + 6–15% (depending on contract with private payer)

Source: Photocure

Valuation assumptions

We model Hexvix/Cysview revenues to Photocure of NOK383m (~$45m) in 2024. We consider this to be very reasonable as there are over 2.8m procedures (which includes both surgical cystoscopies and surveillance cystoscopies) in the addressable market in the US and EU, which adds up to a potential market size of around $3bn (we assume approximately $1,000 per procedure). While patents are set to expire in 2019 in the EU and 2020 in the US, we do not expect immediate generic competition like when a traditional drug becomes generic as any potential competitor would likely need to run some sort of clinical trial and get approval from both the Center for Devices and Radiological Health and the Center for Drug Evaluation and Research due to the nature of Hexvix/Cysview as a drug/device combination. Therefore, even if a competitor starts the process today, the time to initiate a trial, enrol it and obtain approval from regulatory bodies would likely place the earliest time point for a competitive product at 2024 (as a reminder, the original Hexvix pivotal trials took three years, and then you need to allow for filing and regulatory review), and could be far later as the company continues to file for additional patent protection. Additionally, in Europe, there is no clear pathway to approval for a generic drug/device combination and hence the requirements a company is expected to meet are unknown. The additional cost with regards to clinical and regulatory expenses would limit the attractiveness of this market to certain competitors, especially generic competitors, 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.

2 Holowaty et al. *Journal of the National Cancer Institute*, Vol. 91, No.3 February 3, 1999.

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).

The company ran a 262-patient Phase IIb trial comparing three different concentrations of HAL gel (0.2%, 1% and 5%) to placebo in patients with low to moderate grade cervical intraepithelial neoplasia (CIN 1/2). 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, this subgroup of data (from HSIL patients) come from less than 20% of the total intent-to-treat trial population. The company that takes over Cevira would need to either run another Phase II to better understand the risk-reward of a Phase III trial or simply stomach the risk with the understanding that it is moving forward with limited data.

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

3 *Cervical Cancer* by Ruth Dunleavey.
4 Bosch et al., *International Journal of Gynecology and Obstetrics* (2006) 94 (Supplement 1), S8-S21.

to the American College of Pathology, with a similar amount in Europe, making the addressable market around one million.

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.[5] In total, there are an estimated 40–50 million Americans of all age groups who suffer from the condition.[6] 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 8), 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 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. 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.

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

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 the development.

Sensitivities

Photocure is subject to various sensitivities common to healthcare product companies, including commercialisation, competition, reimbursement and patent expiration risks. Hexvix/Cysview is having a surge in sales following approval for the surveillance market, as well as an improvement in reimbursement, but its patent runway is short. Patents are set to expire in September 2019 in the EU and November 2020 in the US, although any potential competitor would likely need to run some sort of clinical trial and get approval from both the Center for Devices and Radiological Health and the Center for Drug Evaluation and Research due to the nature of Hexvix/Cysview as a drug/device combination. This additional cost (both clinical and regulatory) would limit the attractiveness of this market to certain competitors, especially generic competitors, 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. It would also likely be difficult for any competitor to penetrate the market without significant investment in a sales and marketing team.

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 trial exclusively used the Nedax full-face lamp, which may not be readily available in dermatology clinics. 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, more commonly available 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, we arrive at a value for Photocure of NOK1,246m (from NOK970m), or NOK57 per basic share. We have increased our Hexvix/Cysview estimates as we believe there is less risk for competition for the product in the near to intermediate future (we have moved our projected year of generic entry, and hence peak sales, to 2024 from 2020). Our estimate for peak sales is now NOK383m versus NOK295m previously. This may still be conservative as there is currently no indication that any company is making preparations to start the clinical and regulatory work in order to prepare filings for a generic alternative. Also, as the company has indicated it has filed additional patents (likely formulation patents) that could potentially protect the product until 2038, we have extended our model to include that year (previously our model ran through 2029, which seemed sufficient as we had originally expected near-term generic competition).

We have also eliminated Cevira and Visonac from the model as both products continue to be on hold (Visonac has been on hold for over three years and Cevira for over five years) as the company conducts a review of strategic options. If a path forward for either product is announced, we would likely reintroduce it into the model, with any necessary changes. As a reminder, for Cevira, our model had assumed peak penetration of 16% for HSIL cases with sales peaking in 2030 at

NOK2.0bn or around $250m and then falling following the expiration of the method-of-use patent. For Visonac sales peak in 2028 at NOK2.1bn or around $235m. Our model also expected 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.

Additionally, the valuation benefited from an increase in cash following the company achieving operating cash flow positive status during the quarter and NPVs were rolled forward.

Exhibit 9: Photocure valuation summary

Product	Main indication	Status	Probability of commercialisation	Launch year	Peak sales (NOKm)	Peak year	Economics	rNPV (NOKm)
Hexvix/Cysview	Bladder cancer detection	Market	100%	Launched	383	2024	Fully owned – US and Nordics, Partner with Ipsen in EU (35% royalty)	1,139
Total								1,139
Cash and cash equivalents (Q418)								107
Total firm value								**1,246**
Total basic shares (m)								21.8
Value per basic share (NOK)								**57**
Options (Q418, m)								0.0
Total number of shares (m)								21.8
Diluted value per share (NOK)								**57**

Source: Edison Investment Research

Financials

Following Q4 results we have lowered our 2019 revenue estimate from NOK251.0m to NOK240.1m to be a little more conservative, as 2018 results were slightly lower than we had estimated. Our 2019 estimates still represent 32% growth over the NOK181.5m reported in 2018. We have also increased our SG&A estimates from NOK174.5m in 2019 to NOK182.1m as the company is guiding for increased investment in the US sales and marketing organisation. We are also introducing our 2020 estimates, which include NOK294.8m in sales, representing 17% growth over our 2019 estimates. With NOK107m in cash, Photocure should have enough capital to meet its needs prior to profitability, which we currently expect in 2019. Also, importantly, the company was operating cash flow positive in Q418 though we await confirmation that this trend will continue in future quarters.

Exhibit 10: Earnings summary

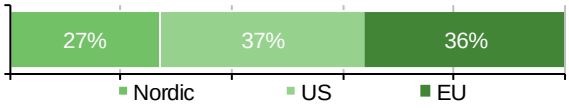
Region	Q418 revenues (NOKm)	2018 revenues (NOKm)	Year-over-year revenue growth in 2018 (%)	Year-over-year in-market unit growth in 2018 (%)
Nordic	13.5	47	9	-4
Partners	14.6	63.3	4*	0*
US	18.4	63.7	50	45
Hexvix/Cysview total	46.3	172.9	16	5

Source: Photocure. Note: *Pro forma, adjusted due to IFRS changes.

Exhibit 11: Financial summary

NOK000s	2017	2018	2019e	2020e
Year end 31 December	IFRS	IFRS	IFRS	IFRS
PROFIT & LOSS				
Revenue	150,911	181,510	240,145	294,796
Cost of Sales	(12,011)	(17,147)	(16,863)	(20,672)
Gross Profit	138,900	164,362	223,282	274,124
Sales, General and Administrative Expenses	(149,098)	(165,530)	(182,083)	(189,366)
Research and Development Expense	(22,896)	(9,325)	(9,697)	(10,085)
EBITDA	(33,094)	(10,492)	31,502	74,672
Operating Profit (before amort. and except.)	(45,202)	(23,703)	18,290	64,103
Intangible Amortisation	0	0	0	0
Other	0	0	0	0
Exceptionals	0	(14,199)	0	0
Operating Profit	(45,202)	(37,902)	18,290	64,103
Net Interest	3,622	1,187	1,235	1,284
Other	0	0	0	0
Profit Before Tax (norm)	(41,580)	(22,516)	19,525	65,387
Profit Before Tax (FRS 3)	(41,580)	(36,715)	19,525	65,387
Tax	6,883	6	(5,272)	(17,655)
Deferred tax	(0)	(0)	(0)	(0)
Profit After Tax (norm)	(34,697)	(22,510)	14,253	47,733
Profit After Tax (FRS 3)	(34,697)	(36,709)	14,253	47,733
Average Number of Shares Outstanding (m)	21.6	21.6	22.0	22.2
EPS - normalised (ore)	(161)	(104)	65	215
EPS - FRS 3 (ore)	(161)	(170)	65	215
Dividend per share (ore)	0.0	0.0	0.0	0.0
BALANCE SHEET				
Fixed Assets	87,486	77,767	65,638	56,173
Intangible Assets	33,315	22,502	8,942	(2,074)
Tangible Assets	1,268	2,141	3,572	5,123
Other	52,903	53,124	53,124	53,124
Current Assets	175,613	153,429	180,117	237,649
Stocks	19,552	18,582	18,582	34,032
Debtors	14,573	20,371	24,014	29,480
Cash	129,368	106,833	129,878	166,494
Other	12,119	7,643	7,643	7,643
Current Liabilities	(40,267)	(52,453)	(52,453)	(52,453)
Creditors	(40,267)	(52,453)	(52,453)	(52,453)
Short term borrowings	0	0	0	0
Long Term Liabilities	(4,752)	(2,401)	(2,641)	(2,905)
Long term borrowings	0	0	0	0
Other long-term liabilities	(4,752)	(2,401)	(2,641)	(2,905)
Net Assets	218,079	176,342	190,661	238,463
CASH FLOW				
Operating Cash Flow	(23,593)	(24,124)	24,128	37,720
Net Interest	0	0	0	0
Tax	0	0	0	0
Capex	(18,588)	(2,188)	(2,253)	(2,321)
Acquisitions/disposals	0	0	0	0
Financing	0	6,339	0	0
Dividends	0	0	0	0
Other	2,310	(2,562)	1,170	1,217
Net Cash Flow	(39,871)	(22,535)	23,045	36,616
Opening net debt/(cash)	(169,239)	(129,368)	(106,833)	(129,878)
HP finance leases initiated	0	0	0	0
Exchange rate movements	0	0	0	0
Other	0	1	0	0
Closing net debt/(cash)	(129,368)	(106,833)	(129,878)	(166,494)

Source: Photocure 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: Daniel Schneider

Dan Schneider joined Photocure in November 2018. He has more than 25 years' experience in developing and expanding rapidly growing healthcare companies in the US, most recently as the general manager for Ablynx in North America. He has also held executive management positions in other pharmaceutical and biotech companies, including BTG International, Somaxon Pharmaceuticals and Sepracor. Mr Schneider holds an MBA from Washington University and a bachelor of science degree in business administration from St Louis University with a double major in finance and marketing.

CFO: Erik Dahl

Erik Dahl joined Photocure in August 2012 as CFO. Most recently, he was CFO for GET, 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.

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.

Vice President Strategic Marketing: Grete Hogstad

Grete Hogstad joined Photocure in February 2005. She has a degree in pharmacy from the University of Oslo, as well as a business degree from the Norwegian School of Management. She has held various leading positions in sales and marketing in Alpharma and Novo Nordisk Pharma, and is a founding member of the Generics Association in Norway.

Principal shareholders	(%)
High Seas AS	10.19
Fondfinans Norge	4.48
KLP Aksje Norge VPF	4.27
Radiumhospitalets Forskningsstiftelse	3.18
Kommunal Landspensjonskasse	3.12
MP Pensjon PK	3.10
Myrlid AS	2.69

Companies named in this report

Nestlé (NESN:VX)

General disclaimer and copyright

This report has been commissioned by Photocure and prepared and issued by Edison, in consideration of a fee payable by Photocure. Edison Investment Research standard fees are £49,500 pa for the production and broad dissemination of a detailed note (Outlook) following by regular (typically quarterly) update notes. Fees are paid upfront in cash without recourse. Edison may seek additional fees for the provision of roadshows and related IR services for the client but does not get remunerated for any investment banking services. We never take payment in stock, options or warrants for any of our services.

Accuracy of content: All information used in the publication of this report has been compiled from publicly available sources that are believed to be reliable, however we do not guarantee the accuracy or completeness of this report and have not sought for this information to be independently verified. Opinions contained in this report represent those of the Edison analyst at the time of publication. Forward-looking information or statements in this report contain information that is based on assumptions, forecasts of future results, estimates of amounts not yet determinable, and therefore involve known and unknown risks, uncertainties and other factors which may cause the actual results, performance or achievements of their subject matter to be materially different from current expectations.

Exclusion of Liability: To the fullest extent allowed by law, Edison shall not be liable for any direct, indirect or consequential losses, loss of profits, damages, costs or expenses incurred or suffered by you arising out or in connection with the access to, use of or reliance on any information contained on this note.

No personalised advice: The information that we provide should not be construed in any manner whatsoever as, personalised advice. Also, the information provided by us should not be construed by any subscriber or prospective subscriber as Edison's solicitation to effect, or attempt to effect, any transaction in a security. The securities described in the report may not be eligible for sale in all jurisdictions or to certain categories of investors.

Investment in securities mentioned: Edison has a restrictive policy relating to personal dealing and conflicts of interest. Edison Group does not conduct any investment business and, accordingly, does not itself hold any positions in the securities mentioned in this report. However, the respective directors, officers, employees and contractors of Edison may have a position in any or related securities mentioned in this report, subject to Edison's policies on personal dealing and conflicts of interest.

Australia

Edison Investment Research Pty Ltd (Edison AU) is the Australian subsidiary of Edison. Edison AU is a Corporate Authorised Representative (1252501) of Myonlineadvisers Pty Ltd who holds an Australian Financial Services Licence (Number: 427484). This research is issued in Australia by Edison AU and any access to it, is intended only for "wholesale clients" within the meaning of the Corporations Act 2001 of Australia. Any advice given by Edison AU is general advice only and does not take into account your personal circumstances, needs or objectives. You should, before acting on this advice, consider the appropriateness of the advice, having regard to your objectives, financial situation and needs. If our advice relates to the acquisition, or possible acquisition, of a particular financial product you should read any relevant Product Disclosure Statement or like instrument.

New Zealand

The research in this document is intended for New Zealand resident professional financial advisers or brokers (for use in their roles as financial advisers or brokers) and habitual investors who are "wholesale clients" for the purpose of the Financial Advisers Act 2008 (FAA) (as described in sections 5(c) (1)(a), (b) and (c) of the FAA). This is not a solicitation or inducement to buy, sell, subscribe, or underwrite any securities mentioned or in the topic of this document. For the purpose of the FAA, the content of this report is of a general nature, is intended as a source of general information only and is not intended to constitute a recommendation or opinion in relation to acquiring or disposing (including refraining from acquiring or disposing) of securities. The distribution of this document is not a "personalised service" and, to the extent that it contains any financial advice, is intended only as a "class service" provided by Edison within the meaning of the FAA (i.e. without taking into account the particular financial situation or goals of any person). As such, it should not be relied upon in making an investment decision.

United Kingdom

Neither this document and associated email (together, the "Communication") constitutes or form part of any offer for sale or subscription of, or solicitation of any offer to buy or subscribe for, any securities, nor shall it or any part of it form the basis of, or be relied on in connection with, any contract or commitment whatsoever. Any decision to purchase shares in the Company in the proposed placing should be made solely on the basis of the information to be contained in the admission document to be published in connection therewith.

This Communication is being distributed in the United Kingdom and is directed only at (i) persons having professional experience in matters relating to investments, i.e. investment professionals within the meaning of Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005, as amended (the "FPO") (ii) high net-worth companies, unincorporated associations or other bodies within the meaning of Article 49 of the FPO and (iii) persons to whom it is otherwise lawful to distribute it. The investment or investment activity to which this document relates is available only to such persons. It is not intended that this document be distributed or passed on, directly or indirectly, to any other class of persons and in any event and under no circumstances should persons of any other description rely on or act upon the contents of this document (nor will such persons be able to purchase shares in the placing).

This Communication is being supplied to you solely for your information and may not be reproduced by, further distributed to or published in whole or in part by, any other person.

United States

The Investment Research is a publication distributed in the United States by Edison Investment Research, Inc. Edison Investment Research, Inc. is registered as an investment adviser with the Securities and Exchange Commission. Edison relies upon the "publishers' exclusion" from the definition of investment adviser under Section 202(a) (11) of the Investment Advisers Act of 1940 and corresponding state securities laws. This report is a bona fide publication of general and regular circulation offering impersonal investment-related advice, not tailored to a specific investment portfolio or the needs of current and/or prospective subscribers. As such, Edison does not offer or provide personal advice and the research provided is for informational purposes only. No mention of a particular security in this report constitutes a recommendation to buy, sell or hold that or any security, or that any particular security, portfolio of securities, transaction or investment strategy is suitable for any specific person.

Frankfurt +49 (0)69 78 8076 960
Schumannstrasse 34b
60325 Frankfurt
Germany

London +44 (0)20 3077 5700
280 High Holborn
London, WC1V 7EE
United Kingdom

New York +1 646 653 7026
1,185 Avenue of the Americas
3rd Floor, New York, NY 10036
United States of America

Sydney +61 (0)2 8249 8342
Level 4, Office 1205
95 Pitt Street, Sydney
NSW 2000, Australia