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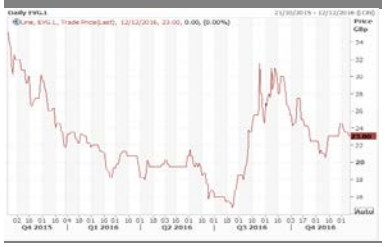
Pharmaceuticals & Biotech



Source: Eikon Thomson Reuters

Market data	
EPIC/TKR	EVG
Price (p)	23.5
12m High (p)	35.0
12m Low (p)	14.5
Shares (m)	73.1
Mkt Cap (£m)	17.2
EV (£m)	10.1
Free Float*	50%
Market	AIM

**As defined by AIM Rule 26*

Description

Evgen is a virtual pharmaceutical company using its proprietary technology, Sulforadex, to create new synthetic and stable variants of the natural product, sulforaphane. Lead product, SFX-01, is now in two Phase II trials

Company information

CEO	Dr Stephen Franklin
CFO	John Bradshaw
Chairman	Barry Clare
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Key shareholders

Directors	3.2%
North West Fund	22.1%
Rising Stars	16.3%
AXA	8.9%
South Yorkshire	5.2%
Seneca	4.8%

Next event

Dec-16	Hardman Initiation
4Q-16	Phase II breast cancer
May-17	Finals
Jun-17	AGM

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Evgen Pharma

Interims – Update on clinical progress

Evgen is a virtual pharmaceutical company focused on the development of a synthetic version of sulforaphane, which is known to modulate key signalling pathways involved in cellular protection and inflammation. Evgen's proprietary technology, Sulforadex, creates new and stable variants of sulforaphane, enabling it to be used as a therapeutic for the first time. Along with interim results, Evgen updated the market on the status of its clinical trials. Lead compound, SFX-01, is in Phase II for subarachnoid haemorrhage (SAH) and a Phase IIa trial has just started in ER+ metastatic breast cancer, with expected read out by end June 2018.

- **Interims**: The update on its clinical trial programme was more important than the actual numbers. However, the company has invested £1.7m during 1H'17, mostly on clinical trials, and ended the period with net cash of £5.5m, which is sufficient to complete the on-going clinical studies at end of fiscal 2018.

- **Phase II in SAH:** Recruitment of the 90 patients in a double-blind, controlled study with SFX-01 is on schedule. Results are expected by end June 2018. Evgen is considering the addition of a second site to accelerate the rate of recruitment. In August 2016, SFX-01 for SAH received Orphan Drug designation in the US.

- **Phase IIa in breast cancer:** Recruitment of 60 patients with hormone resistant ER+ metastatic breast cancer has just commenced at a first site in Belgium, with a further nine sites being added in early 2017. This trial has three cohorts and is an open study design with multiple sites and multiple counties.

- **Neurology:** Good pre-clinical data for SFX-01 versus Tecfidera in a multiple sclerosis model has been reported. Management is expected to make a decision about taking SFX-01 forward either in multiple sclerosis or a smaller neurological indication in early 2017, for which additional funding would be required.

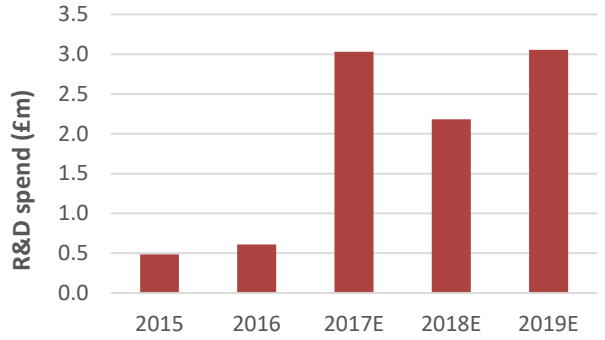
- **Investment summary:** SFX-01 is being targeted initially at conditions which have multi-billion dollar potential and where there is an unsatisfied medical need. There is also potential to use it in other indications. Evgen intends to out-license its drugs to the pharmaceutical majors for global commercialisation. The enterprise value afforded to Evgen by the market does not reflect properly the development stage of SFX-01 and lower than usual risk profile.

Financial summary and valuation

Year end March (£000)	2015	2016	2017E	2018E	2019E
Sales	0	0	0	0	0
SG&A	-312	-338	-980	-1,010	-1,050
R&D	-484	-612	-3,029	-2,181	-3,054
EBITDA	-789	-942	-4,002	-3,183	-4,096
Underlying EBIT	-796	-950	-4,010	-3,191	-4,104
Reported EBIT	-1,246	-2,434	-4,135	-3,322	-4,241
Underlying PBT	-1,853	-1,733	-3,999	-3,187	-4,106
Statutory PBT	-2,303	-3,217	-4,124	-3,318	-4,244
Underlying EPS (p)	-6.2	-3.3	-4.9	-3.9	-5.0
Statutory EPS (p)	-7.8	-6.3	-5.1	-4.1	-5.2
Net (debt)/cash	-903	7,126	3,264	543	-3,221
Capital increases	0	8,565	0	0	0

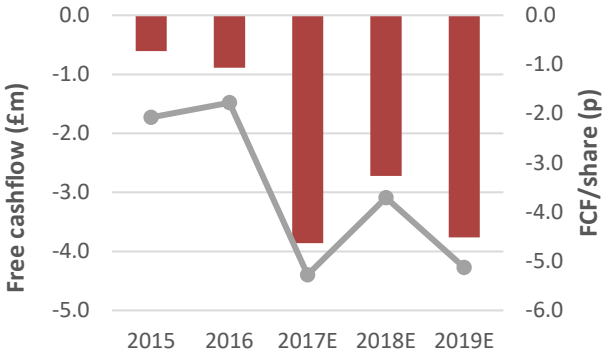
Source: Hardman & Co Life Sciences Research

R&D investment



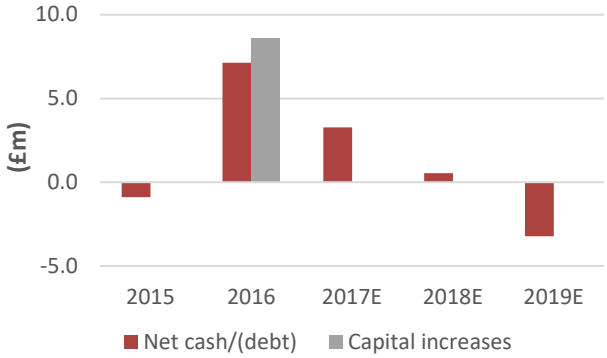
- Investment in R&D has been ramped up to fund the Phase II trial programmes with SFX-01
- Costs have been spread over the expected lifetime of the clinical trial
- Evgen has sufficient funds to complete both Phase II clinical trials with SFX-01 in metastatic breast cancer and subarachnoid haemorrhage

Free cashflow



- Cashflow is driven by the corporate overhead (SG&A) and R&D investment
- Timing differences might occur between accrued tax credits on R&D spend and actual receipts from HMRC

Balance sheet



- Evgen raised £8.5m in fiscal 2016 in a pre-IPO funding round (£2.0m) and at the time of the IPO (£7.0m gross)
- Evgen had net cash of £7.1m at 31st March 2016
- Average monthly burn in fiscal 2017 is ca.£320k

Source: Company data; Hardman & Co Life Sciences Research

Interim results

Evgen is a virtual drug development company focused on the clinical development of pharmaceuticals based on the natural product sulforaphane, which it has stabilised using its Sulforadex technology. SFX-01 is the first stabilised version of sulforaphane that has the potential for use as a therapeutic. The company raised £6.3m net of expenses (£7m gross) at IPO in October 2015 to fund the development of SFX-01 through two Phase II clinical trials in subarachnoid haemorrhage and metastatic breast cancer. Evgen has enough cash to finish both trials, which are expected to report towards the end of the first half of calendar 2018.

Key features

- **Phase II in SAH:** Clinical trial in subarachnoid haemorrhage (SAH) commenced in April 2016. Evgen received Orphan Drug designation in the US and is applying for the designation in Europe
- **Phase II in metastatic breast cancer:** First clinical site (Belgium) is open for recruitment and a minimum of nine further sites will be added early in 2017
- **Strengthened management team:** Two Medical Advisors (ex-AstraZeneca), with speciality in neurology and oncology, have been appointed to support the two on-going Phase II trials
- **R&D investment:** Evgen's reported interim R&D spend of -£1,200k was slightly ahead of our forecast (-£1,100k), indicating the progress being made in its clinical trial programme
- **SG&A:** Following IPO, the management team has been strengthened and the company now has five FTEs. Despite this, the SG&A cost, at -£395k, was lower than our forecast -£500k. However, we believe that the run rate is around £1m per annum
- **Cash burn:** The net loss for the period was -£1.7m which was slightly better than expected. Commencement of the breast cancer trial is expected to see this accelerate in 2H'17
- **Cash position:** The net cash position at 30th September 2016 was £5.5m and was in line with expectations

Interim analysis – actual vs forecast

Interims to end September £'000	1H'16 actual	1H'17 actual	1H'17 forecast	Delta £'000
SG&A	-167	-395	-500	+105
R&D	-200	-1,200	-1,100	-100
Underlying EBIT	**-367**	**-1,595**	**-1,600**	**+5**
Share based payments	-141	-98	-100	+2
Reported operating profit	**-508**	**-1,693**	**-1,700**	**+7**
Net financials	-682	9	5	+4
Underlying pre-tax profit	-1,049	-1,586	-1595	+9
Underlying basic EPS (p)	**-3.4**	**-2.2**	**-2.2**	**-**
Net cash/(debt)	127	5,548	5,540	+8

Source: Company reports; Hardman & Co Life Sciences Research

Clinical trial update

Evgen is progressing two phase II programmes in neurology and oncology with both expected read-out in 1H 2018.

Clinical trial timetable

Drug	Indication	2016	2017	
SFX-01	Metastatic Breast Cancer	Phase II		
SFX-01	Subarachnoid Haemorrhage	Phase II		
SFX-01	Multiple Sclerosis	Preclinical Studies		
New SFX analogues	Various	Preclinical Studies		

Source: Evgen Pharma

Evgen has successfully completed animal safety and toxicology testing with SFX-01 without any adverse effects at the selected therapeutic dose being 300mg twice a day (300mg of SFX-01 corresponds to 46mg of sulforaphane). SFX-01 has been shown to have excellent pharmacokinetics in man and bioavailability of nearly 80% in rats.

Phase II in subarachnoid haemorrhage

Rational

SAH is a life-threatening and catastrophic event caused by bleeding into the space surrounding the brain, the subarachnoid space. It can lead to a debilitating condition caused by oxygen deprivation through cerebral vasospasms and, thus, to impairment of brain function and ultimately tissue death. There has not been any significant clinical advance in SAH in the last 20 years. It is believed that ca.85,000 patients are hospitalised each year in the US and Europe, which represents a huge burden on healthcare systems, with an overall in-patient charge of £510m in UK alone.

SFX-01 is designed to fight against the delayed cerebral ischemia (DCI) due to oxidative stress, that is unpredictable and occurs in 30% of patients 3 to 14 days after the initial haemorrhage. All of these patients would potentially benefit from SFX-01. Based on an estimated price of $20,000 per course of treatment, this would equate to a market opportunity of $1.7bn

Phase II design

Evgen has initiated a Phase II trial in patients suffering an aneurismal subarachnoid haemorrhage, with its first subject recruited in April 2016 at University Hospital Southampton NHS Foundation Trust. It is not attempting to cure blood leakage or prevent SAH, but to prevent the oxidative stress and the toxicity caused by free haemoglobin from the haemorrhage that usually occurs after the brain incident.

The trial will recruit 90 patients in total, with 45 receiving SFX-01 and all the patients receiving nimodipine, the current standard of care. Patients will be administered SFX-01 (300mg bid, corresponding to 92mg of sulforaphane) as capsules or as a suspension *via* a nasogastric tube for up to 28 days, within 48h of experiencing SAH. The read-out is estimated around mid-2018, although the addition of further study sites could expedite this.

Phase II in metastatic breast cancer

The Phase II programme received regulatory approval in August 2016 and is now open for recruitment at a first site in Belgium. The study (NCT02970682) will be multi-country across 10 sites and targets oestrogen positive (ER+) breast cancer patients that are following a hormone based therapy. This trial will investigate SFX-01 in combination with three different hormone-based therapies in 60 ER+ patients, divided equally into three cohorts.

Patients will be partitioned in three cohorts, following their current therapy:

- **Cohort 1**: SFX-01 (300mg twice daily) + Aromatase inhibitors
- **Cohort 2**: SFX-01 (300mg twice daily) + Tamoxifen
- **Cohort 3**: SFX-01 (300mg twice daily) + Fulvestrant

The primary objectives are to evaluate safety and tolerability after up to 24 weeks of dosing with SFX-01, and clinical benefit (tumour size) in patients starting to demonstrate resistance to their hormone therapy. The trial requires a 28 days safety dosing before rolling up to the 24 weeks of dosing. The study read-out is estimated to be mid-2018, although an earlier read-out from one of the arms is possible because the study is 'open label'.

Market size

With a prevalence of nearly 700,000 cases in US and Europe, breast cancer is the most common cancer worldwide. Amongst them, 70% are called oestrogen positive, meaning they are sensitive to hormonal therapy. These cancers usually develop metastases, and hormone therapies are the main treatment and very effective. In 50% of the cases, cancers develop resistance to the therapy, following a mechanism of resistance due to hormone-independent cancer stem cells. SFX-01 has been shown to inhibit breast cancer in both early and metastatic stages in patient-derived xenograft tumours. In 2013, the market was valued at nearly $10bn and it is expected to double in the next 10 years. Assuming a very conservative price of $10,000 p.a. for SFX-01 and the addressable population shown in the table above, the market opportunity in breast cancer would be $4.1bn.

Multiple sclerosis

Evgen has also demonstrated positive results with SFX-01 through the modulation of the oxidative stress in animal models that replicate some features of multiple sclerosis (MS). SFX-01 was shown to have a superior effect compared to the commercially available drug, Tecfidera (Biogen), which is the current standard of care. A strategic review will be undertaken in early 2017 to establish the best way forward for SFX-01 in neurological conditions.

A typical Phase II clinical programme in MS would enrol 120 patients (with a target of 100 completing the study), cost approximatively £10m – much of which is due to repeated imaging costs – and take two years to perform. Alternative chronic neurodegenerative indications (some of which have orphan status) would cost less (ca. £5m) but would still take about two years to perform. Either way, the clinical development of SFX-01 for a chronic neurological condition is unfunded at present. The issue for the Board is whether to pursue the bigger MS market or to develop SFX-01 for smaller chronic neurogenerative diseases, with the potential to obtain Orphan Drug designation, or indeed to continue with just the current two clinical programmes. In our view, Evgen is acutely aware of the dilutive impact of a further round and is therefore committed to exploring sources of non-dilutive capital and/or the potential for an early partnering agreement.

Financial summary

Full financial analysis was provided in our recent publication "*Harnessing the clinical potential of sulforaphane*" dated 29th November 2016.

- **SG&A** – Rise in the corporate overhead cost to ca.£1.0m p.a. as it is now a full quoted company. It is expected that SG&A will only vary modestly given that Evgen is committed to a virtual drug development model with only 5 FTEs
- **R&D** – Investment rises sharply as a consequence of the Phase II trial programme for SFX-01 in SAH (accounting for an estimated 1/3 of the spend) and breast cancer (accounting for 2/3). Trial costs have been allocated evenly across the expected timelines
- **Cashflow** – Cashflow is driven entirely by R&D investment and SG&A spend from the P&L account
- **Net cash** – At the 30th September 2016, Evgen had net cash of £5.55m

Summary financials

Year end March (£000)	2015	2016	2017E	2018E	2019E
Profit & Loss					
Sales	0	0	0	0	0
SG&A	0	-312	-980	-1,010	-1,050
R&D	-445	-484	-3,029	-2,181	-3,054
Licensing/Royalties	0	0	0	0	0
Underlying EBIT	**0**	**-796**	**-4,010**	**-3,191**	**-4,104**
Share based costs	0	-155	-125	-131	-138
Statutory EBIT	0	-1,246	-4,135	-3,322	-4,241
Net financials	0	-1,057	10	4	-3
Underlying PBT	**0**	**-1,853**	**-3,999**	**-3,187**	**-4,106**
Statutory PBT	0	30	85	421	303
Tax liability/credit	0	30	421	303	424
Underlying net income	0	-1,823	-3,578	-2,884	-3,682
Underlying basic EPS (p)	**0.00**	**-6.25**	**-4.89**	**-3.94**	**-5.02**
Statutory basic EPS (p)	0.00	-7.79	-5.06	-4.12	-5.21
Balance sheet					
Share capital	0	73	183	183	183
Reserves	0	-1,260	6,904	3,326	442
Loans & borrowings	1,649	0	0	0	0
less: Cash & deposits	163	7,126	3,264	543	-3,221
Invested capital	**0**	**-284**	**245**	**81**	**163**
Cashflow					
Trading profit	-445	-796	-4,010	-3,191	-4,104
Working capital	0	81	48	41	35
Company op cashflow	**0**	**-708**	**-3,953**	**-3,142**	**-4,061**
Capital expenditure	0	-1	-5	-3	-4
Share issues	0	8,565	0	0	0
Change in net debt	**0**	**-606**	**-3,862**	**-2,720**	**-3,764**
Opening net cash	-297	163	7,126	3,264	543
Closing net cash	**163**	**7,126**	**3,264**	**543**	**-3,221**

Source: Hardman & Co Life Sciences Research

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(Disclaimer Version 2 – Effective from August 2015)

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