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Evgen Pharma

Encouraging interim data from the STEM trial

Evgen (EVG) is a virtual pharmaceutical company focused on the development of a synthetic version of a natural product, sulforaphane, which is known to modulate key signalling pathways involved in cellular protection and inflammation. EVG has created new and stable variants of sulforaphane using its proprietary technology, Sulforadex, enabling it to be used as a therapeutic for the first time. SFX-01 is currently in Phase II trials for both subarachnoid haemorrhage (SAH) and ER+ breast cancer, with read-outs expected around the end of 2018. Meanwhile, EVG has disclosed positive interim data from its STEM trial in metastatic breast cancer.

- **Strategy**: Evgen is focused on the clinical development of synthetic and stable variants derived from sulforaphane using its proprietary technology, Sulforadex. Lead candidate SFX-01 is being assessed in Phase II trials for SAH and breast cancer, both strategic entry portals for other uses in neurology and oncology.

- **Interim data:** Of the 44 patients recruited to date, interim analysis has been performed on 20 patients, who had disease progression prior to starting the trial. Six have seen a beneficial effect of SFX-01 on their tumours, with, four having their disease halted to at least 24 weeks and two to 18 weeks. Furthermore, among them, two show partial response i.e. tumour shrinkage.

- **Positive results:** It is probably too early to draw any firm conclusions, but these initial data provide reassurance that the trial may hit its primary end-point of safety, tolerability and signs of efficacy in this hard-to-treat population. Despite these encouraging data, the share price did not respond as expected.

- **Risks:** As with all drug development companies, there is a risk that products will fail in clinical trials. However, sulforaphane has been through a number of encouraging clinical trials despite its stability and dosing limitations. Therefore, coupled with two potential targets, Evgen's risk profile is arguably reduced.

- **Investment summary:** SFX-01 would be entering multi-billion-dollar global markets that are currently unsatisfied. There is also potential to use sulforaphane in other indications. Evgen intends to out-license its drugs to the pharma majors for commercialisation. Despite some share price appreciation recently, 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)	2016	2017	2018	2019E	2020E	2021E
Sales	0	0	0			
SG&A	-620	-949	-1,063			
R&D	-612	-2,500	-3,250			
EBITDA	-1,224	-3,432	-4,296			
Underlying EBIT	-1,232	-3,449	-4,313			
Reported EBIT	-2,434	-3,658	-4,532	Forecast under review		
Underlying PBT	-2,015	-3,435	-4,307			
Statutory PBT	-3,217	-3,644	-4,526			
Underlying EPS (p)	-3.9	-3.9	-4.6			
Statutory EPS (p)	-6.3	-4.2	-4.8			
Net (debt)/cash	7,126	3,859	2,455			
Capital increase	8,565	0	2,185			

Source: Hardman & Co Life Sciences Research

Pharmaceuticals & Biotechnology

Source: Eikon Thomson Reuters

Market data

EPIC/TKR	**EVG**
Price (p)	21.0
12m High (p)	29.3
12m Low (p)	12.2
Shares (m)	93.3
Mkt Cap (£m)	19.6
EV (£m)	16.0
Free Float*	64%
Market	AIM

**As defined by AIM Rule 26*

Description

Evgen (EVG) 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

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Key shareholders

Directors	2.8%
North West Fund	17.4%
Rising Stars	12.8%
AXA	9.2%
Seneca	7.4%
South Yorkshire	4.0%

Diary

2H'18	SAS trial read-out
2H'18	STEM trial read-out

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Interim Phase II trial update

Clinical update

Evgen has reported some interim data from its STEM (**S**FX-01 **T**reatment & **E**valuation in Patients with **M**etastatic Breast Cancer) trial, investigating its proprietary therapeutic SFX-01 in advanced and metastatic breast cancer patients. The target patient population must be showing resistance to endocrine therapy and disease progression prior to entering the study. They will continue to receive endocrine therapy in addition to SFX-01. Out of a target of 60 breast cancer patients, 44 have been recruited to date, and this interim analysis was performed on the 20 that had completed the trial, by reaching week 24 or by being discontinued due to progression at any of the proceeding 6-weekly scans. The final read-out of the STEM trial is anticipated towards the end of 2018.

SFX-01 is well tolerated and safe

SFX-01 was seen to be well tolerated at the dose used for the trial, i.e. 300mg twice daily, with no patients dropping out of the study. SFX-01 has an excellent safety profile with no serious adverse events recorded so far. This is highlighted by the fact that two of the 20 patients have been on SFX-01 for over a year and one of them is still on the compassionate programme.

Early signs of anti-tumour activity

Interim data indicated that, out of the 20 patients that had disease progression despite hormonal treatment prior entering the trial, six had seen a beneficial effect of SFX-01 in stopping tumour progression:

- The tumour stopped progressing in four patients, providing some evidence of the beneficial effect of SFX-01. This is for the full duration of the 24 week study, which included a favourable scan at week 24. In addition, within this four patient set, two showed a partial response with the shrinkage of their tumours, with one who had the reduction in tumour size of at least 30% on one scan.
- An additional two patients showed disease stabilisation up to the 18 week scan, but then the disease relapsed by the final 24 week scan. One of these was starting to show disease regression in a scan prior to the final scan recorded at 24 weeks

These results are very encouraging for these patients that have very little other treatment option for their cancers. Evgen has been told by their clinical advisors that if at least 20% of patients have their tumour growth halted for the 24 week duration of the study, then they will have an interesting option for these hard-to-treat patient population. It is probably too early to say but, with four patient, out of 20, that have their tumour responding positively to SFX-01, Evgen is on the way to reach this challenging goal.

In addition, EVG has initiated a compassionate use programme for those patients who responded positively at 18 weeks of treatment without disease progression. Six patients have enrolled into the programme so far, with two reaching the one year anniversary, providing confidence that the trial will satisfy one of the primary end-points: safety and tolerability, with efficacy endpoint also looking to be on track.

Clinicians comments

Both clinicians, Dr Sacha Howell the Principal Investigator at the Christie Hospital Manchester and François Duhoux, of University Clinics St-Luc, Brussels, have indicated the excellent safety profile of SFX-01.

Dr Sacha Howell: "*In light of this, these interim results are highly encouraging. Objective responses indicate activity in this setting, and disease stabilisation for 6-12+ months represents clinically meaningful prolongation of response*".

Prof. François Duhoux: "*While we must of course wait for the results of the entire study before making any definitive judgment, in this context I think that the initial results pertaining to efficacy are highly encouraging*".

SFX-01: Phase II in advanced breast cancer

Description of the STEM trial

The STEM programme is a multicentre study, with a total of 14 centres recruiting across the UK and mainland Europe. The trial is being led by the principal investigator, Dr Sacha Howell from the Christie Hospital in Manchester. This study is recruiting advanced breast cancer patients who originally responded to hormone treatment but who then started to show resistance and disease progression. Tumour progression/regression is monitored via six-weekly scans and patients are discontinued from the study as soon as a scan show disease progression.

The primary objective of the open label STEM trial is evaluation of safety, tolerability and signs of efficacy by measuring Clinical Benefit Rate at 24 weeks (this includes the proportion of patients that have either stable disease, a partial response or a complete response through to and including week 24). Patients that show disease progression at any of the six weekly scans are discontinued from the study. The effect of SFX-01 on tumour size is measured by RECIST criteria. SFX-01 (300mg twice daily, corresponding to 92mg of sulforaphane) is being given in combination with three different hormone-based therapies (to which the patient has become resistant and are progressing) in 60 ER+ patients 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

Although this trial is quite broad, open label, and enrols patients who are 'quite poorly', the outcomes will allow a better decision to be made regarding the subsequent Phase II trial.

SFX-01 as an anti-cancer agent

During the last 12 months, there has been an increasing number of scientific research papers demonstrating that sulforaphane, the active ingredient of SFX-01, is an effective chemo-protective and therapeutic agent against a vast number of tumours. Sulforaphane is thought to exert its cytoprotective properties through the modulation of enzymes that are active in the initiation phase of carcinogenesis. Importantly, sulforaphane has been proven to stop the cell cycle at the G2/M stage by inhibiting cell proliferation in a dose-dependent manner in xenograft and cellular cancer models, ultimately triggering cell apoptosis and suppressing angiogenesis and metastasis.

Also, new studies from the Manchester Research Centre (MRC) have highlighted the effect of SFX-01 in inhibiting the STAT3 (Signal Transducer and Activator of Transcriptase 3) signalling pathway. STAT3 is a transcription activator that plays a crucial role in many cellular processes seen in cancer and autoimmune disease.

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(Disclaimer Version 4 – Effective from January 2018)

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The fact that we are commissioned to write the research is disclosed in the disclaimer, and the research is widely available.

The full detail is on page 26 of the full directive, which can be accessed here: http://ec.europa.eu/finance/docs/level-2-measures/mifid-delegated-regulation-2016-2031.pdf

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