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This document is an AIM admission document and has been drawn up in accordance with the AIM Rules for Companies. This document does not constitute a prospectus within the meaning of section 85 of FSMA, has not been drawn up in accordance with the Prospectus Rules and has not been approved by or filed with the Financial Conduct Authority (the ''FCA''). This document does not constitute an offer of transferable securities to the public within the meaning of FSMA or otherwise.

The Directors of the Company, whose names appear on page 5 of this document, accept responsibility, collectively and individually, for the information contained in this document, including individual and collective responsibility for compliance with the AIM Rules for Companies. To the best of the knowledge of the Directors (having taken all reasonable care to ensure such is the case) the information contained in this document is in accordance with the facts and contains no omission likely to affect the import of such information.

Application has been made for the Enlarged Share Capital to be admitted to trading on AIM, a market operated by the London Stock Exchange. It is expected that Admission will become effective and dealings in the Ordinary Shares will commence on 21 October 2015.

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The whole of the text of this document should be read. You should be aware than an investment in the Company involves a high degree of risk. Your attention is drawn to the risk factors set out in Part II of this document.

EVGEN PHARMA PLC

Incorporated and registered in England and Wales with registered number 09246681

Placing of 18,918,919 ordinary shares of £0.0025 each at 37p per ordinary share

and

Admission to trading on AIM

Nominated Adviser and Broker

The New Ordinary Shares will, on Admission, rank *pari passu* in all respects with the Existing Ordinary Shares including the right to receive all dividends or other distributions declared, paid or made after Admission.

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Copies of this document will be available free of charge to the public during normal business hours on any day (Saturdays, Sundays and public holidays excepted) at the offices of Northland Capital from the date of this document for the period ending one month after Admission.

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KEY INFORMATION

The following information is extracted from, and should be read in conjunction with, the full text of this document. Investors should read the whole document and not rely solely on the information in this "Key Information" section or any other information summarised in this document.

Overview

Evgen Pharma is a clinical stage drug development company. The Group's objective is to establish a dominant position in the development of pharmaceuticals based upon sulforaphane and related analogues. Evgen Pharma is developing novel therapies for specific cancers (e.g. breast cancer) and neurological diseases such as subarachnoid haemorrhage (a type of stroke) and multiple sclerosis.

The Group's core technology is Sulforadex®, a means of synthesising and concurrently stabilising sulforaphane or, as more recently demonstrated, novel analogues based upon sulforaphane. Sulforaphane is a plant-derived small molecule with established anti-cancer properties and is a known activator of the Nrf2 pathway. Sulforaphane's clinical and commercial development has, to date, been precluded by the instability of the molecule.

The Group utilises its Sulforadex® technology to develop products that exploit the therapeutic properties of sulforaphane and related analogues. The Group's first development product, SFX-01, has completed Phase I trials and has been demonstrated to be safe and well tolerated.

Evgen Pharma's strategy is to simultaneously target relatively rare diseases with the potential for orphan designation and conditional marketing authorisations (where a more rapid market approval is possible), alongside larger markets with conventional drug development timelines. This dual track approach affords the Group a balance between the potential for early revenue and the later-stage larger returns predicated on success in major therapeutic markets.

The Group has engaged a CRO prior to starting a Phase II trial in subarachnoid haemorrhage.

The Directors believe that the Group has the following key strengths:

- a lower risk profile for an early stage drug development company, due to the wealth of published scientific literature concerning the anti-cancer activities and neuroprotective effects of sulforaphane;
- it operates with a capital efficient business model;
- a broad intellectual property position in terms of novel compositions and processes; and
- a highly experienced management team.

Placing and use of proceeds

The Company is seeking to raise £6.3 million (net of expenses) through the Placing of the New Ordinary Shares. Application has been made to the London Stock Exchange for the Existing Ordinary Shares and the New Ordinary Shares to be admitted to trading on AIM, which is expected to occur on 21 October 2015. The net proceeds of the Placing will be used:

- to fund a Phase IIa clinical trial on SFX-01 in metastatic breast cancer;
- to enhance and accelerate a Phase II clinical trial on SFX-01 in subarachnoid haemorrhage;
- to fund long-term safety and toxicology studies on SFX-01;
- to fund preclinical studies on SFX-01 in models of multiple sclerosis;
- to fund an assessment and early preclinical development of novel sulforaphane analogues;
- to expand existing, or initiate new, preclinical or clinical work programmes as deemed appropriate by the Board; and
- for working capital purposes (including IP costs and licence fees).

YOUR ATTENTION IS DRAWN TO THE RISK FACTORS SET OUT IN PART II OF THIS DOCUMENT

PLACING AND ADMISSION STATISTICS

Placing Price	37p
Number of Existing Ordinary Shares	53,951,943
Number of New Ordinary Shares to be issued pursuant to the Placing	18,918,919
Number of Ordinary Shares in issue immediately following Admission	72,870,862
Number of Ordinary Shares the subject of options, Warrants or LTIP IPO Awards	10,202,669
Percentage of the Enlarged Share Capital represented by the Placing Shares	26 per cent.
Estimated gross proceeds of the Placing receivable by the Company	£7.0 million
Estimated net proceeds of the Placing receivable by the Company	£6.3 million
Market capitalisation of the Company at the Placing Price at Admission	£27.0 million
TIDM	EVG
ISIN	GB00BSVYN304
Website	www.evgen.com

EXPECTED TIMETABLE OF PRINCIPAL EVENTS

Publication of this document	15 October 2015
Issue of Placing Shares, Admission of Enlarged Share Capital and commencement of dealings in the Enlarged Share Capital on AIM	8.00 a.m. on 21 October 2015
CREST accounts credited in respect of Ordinary Shares	8.00 a.m. on 21 October 2015
Despatch of definitive share certificates, where applicable	by 28 October 2015

References to times and dates in the timetable above are to London, UK time, unless otherwise stated. Each of the times and dates in the above timetable is subject to change without further notice.

DIRECTORS, SECRETARY AND ADVISERS

Directors	Barry Clare, *Executive Chairman* Dr Stephen Joseph Franklin, *Chief Executive* John Bradshaw, *Finance Director* Dr Susan Elizabeth Foden, *Non-Executive Director* Dr Mark Andrew Wyatt, *Non-Executive Director* Dr Marc François d'Abbadie, *Non-Executive Director* Dr Alan John Barge, *Non-Executive Director*
Company Secretary	John Bradshaw
Registered Office of the Company	Liverpool Science Park Innovation Centre 2 146 Brownlow Hill Liverpool Merseyside L3 5RF
Nominated Adviser and Broker	Northland Capital Partners Limited 131 Finsbury Pavement London EC2A 1NT
Solicitors to the Company	Pinsent Masons LLP 30 Crown Place London EC2A 4ES Theobald Associates 16 St Martin's le Grand St Paul's London EC1A 4EN
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PART I

INFORMATION ON THE GROUP

Business overview

Evgen Pharma is a clinical stage drug development company. The Group's objective is to establish a dominant position in the development of pharmaceuticals based on sulforaphane and related analogues. Evgen Pharma is developing novel therapies for specific cancers (e.g. breast cancer) and neurological diseases such as subarachnoid haemorrhage (a type of stroke) and multiple sclerosis.

The Group's core technology is Sulforadex®, a means of synthesising and concurrently stabilising sulforaphane or, as more recently demonstrated, novel analogues based upon sulforaphane. Sulforaphane is a plant-derived small molecule with established anti-cancer properties and is a known activator of the Nrf2 pathway. Sulforaphane's clinical and commercial development has, to date, been precluded by the instability of the molecule.

The Group utilises its Sulforadex® technology to develop products that exploit the therapeutic properties of sulforaphane and related analogues. The Group's first development product, SFX-01, has completed Phase I trials and has been demonstrated to be safe and well tolerated.

Evgen Pharma's strategy is to simultaneously target relatively rare diseases with the potential for orphan designation and conditional marketing authorisations (where a more rapid market approval is possible), alongside larger markets with conventional drug development timelines. This dual track approach affords the Group a balance between the potential for early revenue and the later-stage larger returns predicated on success in major therapeutic markets.

The Group has engaged a CRO prior to starting a Phase II trial in subarachnoid haemorrhage.

The following table summarises the status of the Group's product pipeline:

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

In addition to the above pipeline, the Company is currently negotiating a worldwide, exclusive licence from the Spanish National Research Council (CSIC) and the University of Seville to intellectual property rights associated with novel sulforaphane analogues. The Directors believe that this licence agreement will be executed before 1 December 2015.

The Directors believe the Group has the following key strengths:

- a lower risk profile for an early stage drug development company, due to the wealth of published scientific literature concerning the anti-cancer activities and neuroprotective effects of sulforaphane;
- it operates with a capital efficient business model;
- a broad intellectual property position in terms of novel compositions and processes; and
- a highly experienced management team.

The Placing will raise approximately £7 million for the Company (approximately £6.3 million, net of expenses) through the placing of 18,918,919 New Ordinary Shares with institutional and other investors. Application has been made to the London Stock Exchange for the Enlarged Share Capital to be admitted to trading on AIM, which is expected to occur on 21 October 2015. The net proceeds of the Placing will be used to fund the Group's clinical stage programmes on SFX-01,

long-term safety and toxicology studies on SFX-01, further preclinical development programmes (on SFX-01 and exploratory new analogues) and provide the Group with working capital.

History and background

The Group commenced operations in January 2008, when Evgen was founded by Dr Stephen Franklin in collaboration with two venture capital investors, Enterprise Ventures and Imprimatur Capital. Evgen was established as an entrepreneur-led (as opposed to academic-led) initiative with Dr Franklin being given a mandate to conduct a global search and screen programme with a view to identifying a new technology, underpinned by robust intellectual property, that could have a disruptive impact in the healthcare market. This process resulted in the identification and validation by Evgen of the commercial opportunity associated with the exploitation of the established but unstable anti-cancer agent, sulforaphane. Sulforaphane, and its potential therapeutic benefits, is frequently referenced in the popular press in the context of its most common botanical source, brassica vegetables, such as broccoli.

Key intellectual property rights pertaining to the successful stabilisation of sulforaphane were in-licensed by Evgen, on a worldwide exclusive basis, from co-owners PharmAgra and Lalilab. PharmAgra is a custom chemical synthesis company based in North Carolina, United States. Lalilab, also based in North Carolina, is a company that supplies high quality raw materials to the pharmaceutical and food industries.

Evgen branded the stabilised sulforaphane technology, Sulforadex®, and began building its pharmaceutical development capability. Evgen initially focused on developing its lead product, SFX-01, as a treatment for low-grade localised prostate cancer. It subsequently widened its activity to include potential applications of SFX-01 in breast cancer and a type of stroke, subarachnoid haemorrhage.

Following a strategic review in 2015, breast cancer and subarachnoid haemorrhage were selected as the most appropriate trials to target first, given the relative risk profiles of the different programmes and the stage of development of the Group. Whilst prostate cancer remains a major market opportunity of great interest, the Directors have taken the decision to defer development in this area.

PharmAgra has an FDA-accredited manufacturing facility and manufactures SFX-01 under license for clinical trial purposes. The Group controls all manufacturing rights and can select the appropriate suppliers for future commercialisation.

From January 2008 to July 2015, the Group raised a total of £4.2 million from a mixture of venture capital, other institutional investors, high net-worth individuals and grant financing from the Technology Strategy Board (now Innovate UK).

These funds have been primarily used to advance the Group's lead product, SFX-01 through:

- preclinical safety and toxicology programmes;
- a first-in-man Phase I trial, using a single ascending dose in healthy volunteers to establish safety and tolerance; and
- a second Phase I trial using a multiple ascending dose in healthy volunteers to establish safety and tolerance.

The Company raised an additional £2 million of equity in the Pre-IPO Round in August 2015. These funds enabled the Group to engage with a CRO prior to starting the Group's first Phase II trial.

In addition to the Sulforadex® technology, the Group has recently issued a formal notice to exercise an option to license the worldwide exclusive rights to intellectual property associated with novel sulforaphane analogues from the Spanish National Research Council (CSIC), in collaboration with the University of Seville. These intellectual property rights should help the Group defend itself from competition and will give the Group the opportunity to segment diverse oncology and neurological markets. The initial analogues from this collaboration are at an early stage of discovery. The Directors expect that the Group will conduct preclinical testing on these and further analogues arising from this collaboration.

Key Strengths

Clinical stage drug development company with a lower risk profile

The Directors believe the Group has a lower risk profile for an early stage drug development company because:

- there is a wealth of published peer-reviewed scientific papers regarding the anti-cancer and anti-inflammatory properties of sulforaphane, the active molecule within SFX-01;
- SFX-01 has been demonstrated by the Group to be safe and well tolerated, with excellent bioavailability in trials on healthy human volunteers; and
- SFX-01 will be advanced in two clinical trials (breast cancer and subarachnoid haemorrhage) and one preclinical programme (multiple sclerosis), thereby mitigating risk of clinical failure.

Capital efficient business model

The Directors believe the Group operates on a capital efficient basis because it outsources manufacturing and clinical development to specialist contract manufacturing organisations and CROs, respectively. The Group operates, and will continue to operate, a virtual drug development business model with a small core team of employees.

Broad intellectual property position

The Group was established to identify a major market opportunity underpinned by a broad IP position. Part IV of this document contains a report by HGF on the Group's intellectual property portfolio. The Directors are mindful of the fact that successful drugs tend to be refined through medicinal chemistry and competitors may focus on new analogues to bypass the Group's IP. To mitigate this, the Group has secured an exclusive option from the Spanish National Research Council (CSIC), in collaboration with the University of Seville, to negotiate a worldwide licence of intellectual property with new composition of matter claims over a wide range of sulforaphane-based analogues.

Highly experienced management team

The management team combines a blend of public company experience (small and large capitalisation) with a high level of scientific excellence and clinical development experience. Further details of the senior management team and their biographies can be found below in the section headed, 'Directors, Senior Management and Employees'.

The Group's Technology

Growth in sulforaphane science

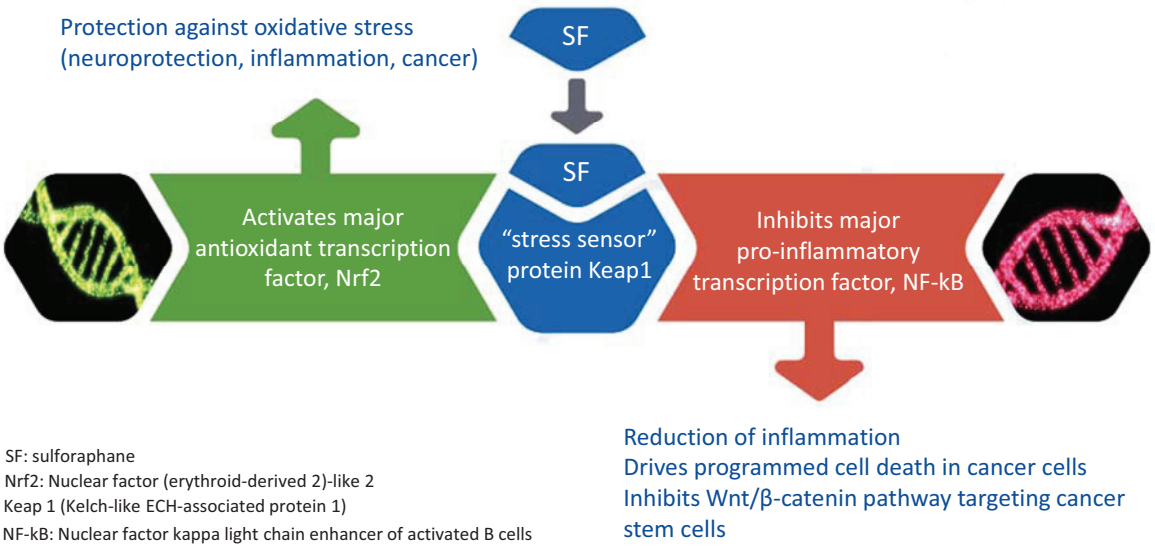
There is a significant body of scientific data that demonstrates the anti-cancer properties of sulforaphane in all three phases of cancer (tumour initiation, promotion and progression). Sulforaphane, which is derived from glucoraphanin (a molecule of botanical origin, and found in brassica vegetables such as broccoli), has a large body of peer-reviewed scientific publications containing compelling evidence for its biological efficacy (*in vitro* and *in vivo*) in academic research. There are over 500 peer-reviewed scientific publications specifically dedicated to its anti-cancer properties. Sulforaphane has been shown to reduce proliferation and induce programmed cell death in many cancers including prostate, breast, pancreatic, and lung cancer and some haematological malignancies such as acute lymphoblastic leukaemia.

Sulforaphane is known to modulate two biochemical pathways, Nrf2 and NF-kB, that have been implicated in both cancer and neurodegenerative disease. Whilst the anti-cancer effects of sulforaphane have been established since 1992, the neuroprotective effects of sulforaphane have more recently gained traction in published scientific literature. In recent years, sulforaphane has been shown in *in vitro* and *in vivo* studies to have neuroprotective effects in ischaemic stroke, traumatic brain injury, multiple sclerosis, Alzheimer's disease and Parkinson's disease.

The published scientific literature on sulforaphane's mechanism of action has largely focused on its ability to upregulate the transcription factor, Nrf2 (which drives the antioxidant response) and downregulate the transcription factor, NF-kB (which drives an inflammation response). Using Nrf2 animal models (with the Nrf2 gene ''knocked out''), it has been possible to demonstrate that the neuroprotective effect of sulforaphane following a brain haemorrhage is linked to this specific pathway. The Nrf2 and NF-kB pathways are commonly cited mechanisms by which sulforaphane exerts its therapeutic effect (see Figure 1 below), although other targets have been implicated and

include HDAC inhibition and inhibition of cancer stem cell survival via the Wnt/beta-catenin pathway (either directly and/or indirectly via NF-kB).

Figure 1: Sulforaphane mechanism of action: binding to Keap 1, activating Nrf2 and inhibiting NF-kB



Despite the growth of evidence in the scientific literature, the Directors are not aware of any clinical studies having been performed by third parties on pure synthetic sulforaphane. The Directors believe that this is because sulforaphane, when chemically synthesised, is a liquid that needs to be stored and shipped at -20°C, typically under an inert gas, to maintain stability and this makes it difficult to store and administer to humans.

The Directors conducted a search and, as far as they are aware, the only registered clinical trials relating to sulforaphane have been conducted on botanical extracts that contain the sulforaphane precursor molecule (glucoraphanin) or have been enzymatically treated to release sulforaphane from the precursor molecule and then subsequently frozen (or in one instance refrigerated) prior to administration in the clinic.

Whilst these trials demonstrate a clinical desire to test sulforaphane, the Directors are not aware of any third party development of a product directed at gaining regulatory approval as a pharmaceutical.

Sulforadex® Technology

The Sulforadex® technology is a means of synthesising and concurrently stabilising sulforaphane or, as more recently demonstrated, novel analogues based upon sulforaphane.

The lead product, SFX-01, comprises a synthetic sulforaphane molecule within an α-cyclodextrin complex. SFX-01 is manufactured using a proprietary (supported by patent applications with geographical reach into the major manufacturing economies) two-step chemical process, starting with a small molecule chemical intermediate called erucin (see Figure 2 below). The α-cyclodextrin acts as both a catalyst for the synthesis of the sulforaphane and, as the reaction conditions are altered, the formation of the scaffold renders the sulforaphane stable and in solid form.

This innovation has enabled the development of a scaleable manufacturing process and a resultant active pharmaceutical ingredient ("API") with ICH stability data running out to two years, in stark contrast to the instability of regular sulforaphane (see Figure 3 below). The significance of this stable powder API, together with the GRAS status of α-cyclodextrin, and the favourable manufacturing economics, means that, for the first time, a regular capsule or tablet pharmaceutical sulforaphane product is viable.

Figure 2: Sulforadex® technology: a means of synthesising and concurrently stabilising sulforaphane or related analogues

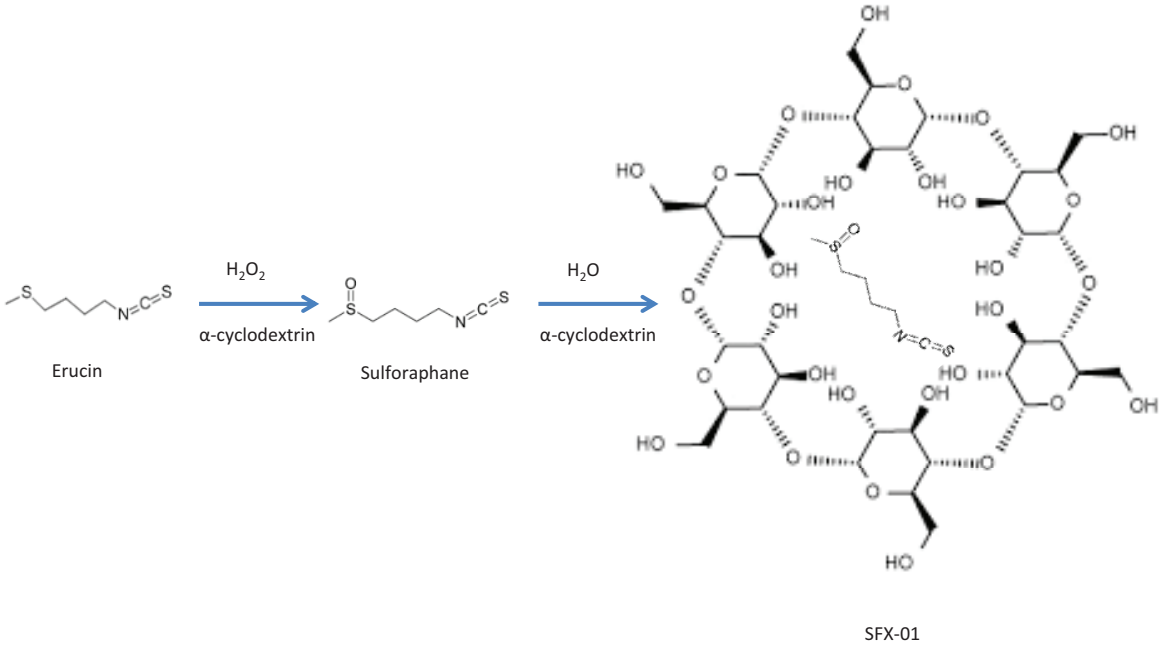
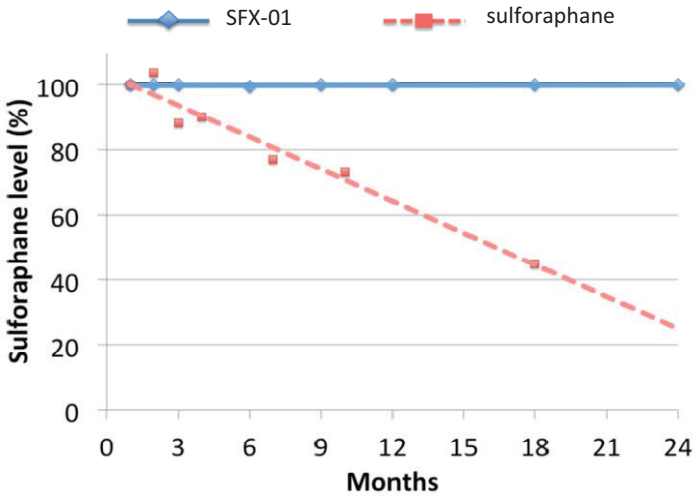


Figure 3: Pharmaceutical standard stability data for lead product SFX-01 (a combination of sulforaphane and α-cyclodextrin)



The Directors believe the Group's Sulforadex® technology represents a major breakthrough in harnessing the clinical potential of sulforaphane (and related analogues) as a potential therapy in cancer, neurology and other diseases characterised by oxidative stress and inflammation.

SFX-01 has been shown to have excellent pharmacokinetics in man, with a bioavailability of approximately 80 per cent. When the sulforaphane is released from the α-cyclodextrin, it has the same half-life in the body as regular sulforaphane, and has been demonstrated to be equipotent to regular sulforaphane in all head-to-head tests undertaken by the Group (breast cancer, acute lymphoblastic leukaemia and COPD).

The published *in vitro* and *in vivo* evidence for sulforaphane efficacy in cancer has been sufficient to underpin the Group's previous clinical trial approvals from the MHRA (for the Group's Phase I trials). In the field of breast cancer, the Group has established a collaboration with the Cancer Research UK Manchester Institute to build a new preclinical evidence base for SFX-01 (as opposed to relying on third-party published scientific literature relating to sulforaphane). This

collaboration has recently demonstrated that in mouse xenograft models (with both early stage patient-derived tissue and later stage metastatic tissue), SFX-01 decreases cancer stem cell populations; the implication being that SFX-01 may have a therapeutic role, in combination with endocrine therapy, in treating advanced metastatic breast cancer.

The Group's Objective and Strategy

The Group's objective is to establish a dominant position in the development of pharmaceuticals based upon sulforaphane and related analogues. The Group's strategy to achieve this objective is to:

- focus internal resources in the fields of oncology and neurology;
- pursue near and longer-term revenue generation opportunities by targeting both mass market indications and those with the potential for orphan designation and conditional marketing approval;
- seek to license clinical assets after completing Phase II trials;
- expand its intellectual property portfolio, including specific dose regimes, product formulations and new uses, where such protection is possible;
- seek to control, and where appropriate, develop intellectual property pertaining to new composition of matter around sulforaphane analogues; and
- appraise acquisition and in-licensing opportunities outside of Sulforadex®, with a view to diversifying the product pipeline, where the Directors believe such opportunities have a good strategic fit.

The Group's Development Products

The Group's first development product based on Sulforadex® is SFX-01, which has completed Phase I trials and has been demonstrated to be safe and well tolerated. SFX-01 is now ready to be advanced into two patient trials, a Phase IIa trial in metastatic breast cancer and a Phase II trial in subarachnoid haemorrhage. The net proceeds of the Placing will enable the initiation of the Phase IIa trial in metastatic breast cancer and the expansion and acceleration of the Phase II trial in subarachnoid haemorrhage.

The net proceeds of the Placing will also be used by the Group to test SFX-01 in preclinical models of multiple sclerosis and to complete fertility and reproductive toxicology studies. In addition, the net proceeds will be used to undertake a preclinical assessment of a range of novel sulforaphane analogues.

The following table summarises the status of the Group's product pipeline:

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

In addition to the above pipeline, the Company is currently negotiating a worldwide, exclusive licence from the Spanish National Research Council (CSIC) and the University of Seville to intellectual property rights associated with novel sulforaphane analogues. The Directors believe that this licence agreement will be executed before 1 December 2015.

Metastatic breast cancer

In the metastatic setting, endocrine therapies are the mainstay of treatment for ER+ breast cancer. In the pre-menopausal population the standard of care in the absence of previous endocrine

therapy is tamoxifen with or without ovarian suppression. If tamoxifen has been used previously then ovarian suppression plus an aromatase inhibitor is preferred. In post-menopausal women, the standard of care is a third generation aromatase inhibitor although the selective estrogen downregulator, fulvestrant, is a viable first line treatment or can be used after relapse from adjuvant aromatase inhibitor therapy. When second or third-line hormonal therapy has failed, the only option for most patients is chemotherapy.

One proposed mechanism for the generation of resistance to endocrine therapy is the proliferation of a hormone-independent clone of breast cancer stem cells (''CSCs''). Such cells are known to proliferate during treatment with hormonal agents, and can engender a clone of hormone-resistant progenitors which can then repopulate the tumour and render it hormone-independent.

Previously published data has shown that sulforaphane can inhibit breast CSCs. SFX-01 has been shown, by the Group, to inhibit breast CSC activity of both early-stage and metastatic patient-derived xenograft (''PDX'') tumours and could therefore potentially produce clinically meaningful improvements to endocrine therapy. The Directors believe that SFX-01 has the potential to be a well-tolerated treatment which may prevent the onset of resistance in early breast cancer, thus increasing chances of cure, and significantly delaying the onset of hormone resistance in both pre and post-menopausal women in the advanced metastatic setting.

The objective of SFX-01 therapy is to reduce the number of CSCs proliferating in those tumours which are treated with anti-hormonal agents, and prolong the duration of response. The proposed clinical study is a randomised study in patients with ER+ metastatic breast cancer who have failed on prior adjuvant, or first-line aromatase inhibitor therapy. The proposed study is risk-managed, with a Phase IIa component comprising 40 patients. This will allow for an early efficacy signal based on tumour volume, to determine if there is preliminary evidence of efficacy. Provided that there is evidence of activity, the intention (subject to further funding) is to advance SFX-01 into a Phase IIb trial in 160 patients, with progression-free survival as the primary clinical endpoint.

Subarachnoid haemorrhage

A subarachnoid haemorrhage (''SAH'') is a bleed into the subarachnoid space around the outside of the brain. This may occur spontaneously, usually from a ruptured cerebral aneurysm (c. 85% of cases), or may result from head injury. SAH is a rare disease which could lead to an orphan designation for SFX-01 by the regulatory authorities.

Conventional treatment for SAH is primarily directed to securing the aneurysm to prevent a further re-bleed. However, this treatment does nothing to ameliorate the morbidity and mortality caused by the subsequent cerebral ischaemia; the only effective treatment for which is nimodipine. The efficacy of nimodipine as a treatment for SAH is limited and, despite its use, poor outcomes remain a significant problem as evidenced by contemporary outcome data since its introduction. Moreover, even in the survivors of SAH, conventionally considered to have made a good recovery, neurocognitive deficits are common, leading to extensive problems with social reintegration and functioning in the workplace.

The mechanisms underlying poor outcomes are multifactorial. A significant component is due to secondary injury from inflammation, spreading depolarisation, delayed cerebal ischaemia and microcirculatory disturbance. The common factor in all these mechanisms is that they are initiated by extracellular haemoglobin released as red blood cells breakdown. This results in direct neurotoxicity and increased oxidative stress and further injury. Thus any treatment to ameliorate their effects would be best targeted at reducing the cell free haemoglobin, oxidative stress and inflammation.

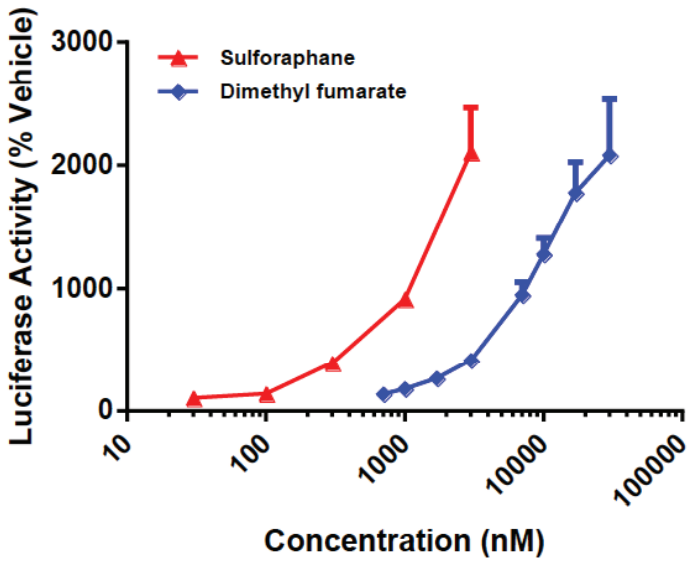
Sulforaphane is known to upregulate the Nrf2 pathway. Nrf2 is a promoter of haptoglobin expression and a wide range of anti-oxidant and anti-inflammatory enzymes including Haeme Oxygenase-1 (HO-1) and NAD(P)H:quinone oxidoreductase-1 (NQO1). These effects have been shown to reduce inflammation and neurological deficits seen in rats after intracerebral haemorrhage and SAH.

The objective of the therapy is co-administration with standard-of-care nimodipine, to reduce the vasospasm and incidence of delayed cerebral ischaemia following subarachnoid haemorrhage. The net proceeds of the Placing will allow the Group to advance SFX-01 through an enhanced and accelerated Phase II clinical trial (c 90 patients) for subarachnoid haemorrhage that has been statistically powered to support a potential conditional market approval. This trial represents a potentially faster route to a marketable product that could drive early licence revenue from 2018.

Multiple Sclerosis

The net proceeds of the Placing will allow the Group to advance a comprehensive preclinical study on SFX-01 in two models of relevance to both the relapsing-remitting and progressive form of multiple sclerosis. This study will compare the efficacy of SFX-01 against the active ingredient (dimethyl fumerate) from Biogen IDEC's Tecfidera. The Group is encouraged by previously published data that has shown that sulforaphane, the active ingredient of SFX-01, is a more potent activator of Nrf2 than dimethyl fumerate, the active ingredient of Tecfidera. (See Figure 4 below).

Figure 4: Nrf2 potency in a rat hepatoma cell line



Source: Reproduced with the permission of Dr Ian Copple, MRC Centre for Drug Safety Science, Dept. of Molecular & Clinical Pharmacology, The University of Liverpool, UK. Data presented at the The Keap1/Nrf2 Pathway in Health and Disease, 6—8 January 2015, Robinson College, Cambridge, UK

Sulforaphane has also been shown to ameliorate relapsing EAE (Experimental Autoimmune Encephalomyelitis), a model of multiple sclerosis. However, this published study used a high dose of sulforaphane and it did not explore the progressive form of EAE. The proposed preclinical programme will study the effect of SFX-01 in two animal models of EAE: MOG35-55 C57BL6 model and the Biozzi ABH CREAE model. The Directors believe that these two models give insight into potential clinical efficacy for both the relapsing-remitting and progressive forms of the disease.

New sulforaphane analogues

On 1 September 2015, the Group gave notice to the University of Seville and CSIC to exercise the option to negotiate a worldwide exclusive licence agreement. Headline commercial terms in respect of the licence are described in the option agreement. The net proceeds of the Placing will also allow the Group to undertake exploratory preclinical studies to ascertain efficacy and safety of these new analogues.

Other

The Group will also continue its ongoing safety programme on SFX-01 by completing fertility and reproductive toxicology studies.

The Group's Collaborators and Clinical Relationships

The Group has built collaborative relationships with clinicians, across three disease areas, relating to the near-term clinical trials in breast cancer and subarachnoid haemorrhage, and also in prostate cancer.

Clinical programme	Principal Investigator	Institution
Breast Cancer	Dr Sacha Howell. Senior Lecturer and Honorary Consultant Medical Oncologist	Cancer Research UK Manchester Institute, Manchester, UK
Subarachnoid Haemorrhage	Diederik Bulters, Consultant Neurosurgeon	University Hospital Southampton, Southampton, UK
Prostate Cancer	Dan Lin MD, Professor of Urology and Joshi Alumkal MD, Associate Professor of Medicine and Co-Leader Prostate Cancer Research Program	University of Washington Medical Center, Seattle, Washington State in collaboration with the Knight Cancer Institute, Oregon Health and Science University, Portland, Oregon, US

The Group also has a number of preclinical research collaborations, with the objective of building the body of data around SFX-01's mechanism of action, and the potential expansion of the clinical utility of SFX-01 or new analogues.

Preclinical collaborations

Start of collaboration	Institution	Objective
2012	Paterson Institute for Cancer Research, Manchester, UK	*In vitro* and *in vivo* effects of SFX-01 on breast cancer stem cells and mechanism of action
2013	Baylor College of Medicine, Texas Children's Hospital, Houston, Texas, US	*In vitro* and *in vivo* effects of SFX-01 in Acute Lymphoblastic Leukaemia (ALL)
2013	King's College, University of London, UK	Identification of SFX-01 molecular targets using an antibody that recognises sulforaphane-protein adducts
2013	Royal Veterinary College, University of London, UK	Effect of SFX-01 on *in vivo* model of osteoarthritis joint disease
2014	Duke University, Durham, North Carolina, US	Effect of SFX-01 on *ex vivo* model of sickle cell anaemia
2014	University of Liverpool, UK	Mechanism of action of SFX-01 and other sulforaphane analogues using an Nrf2 *in vivo* model
2015	Mayo Clinic, US	Regenerative medicine: repair of bone, cartilage, ligament and tendon tissue
Planned for late 2015	University of Southampton, UK	Testing of SFX-01 in multiple sclerosis *in vivo* models vs dimethyl fumarate

Market Overview

Introduction

The initial target market for SFX-01 within oncology is metastatic ER+ breast cancer in combination with endocrine therapy.

The initial target markets for SFX-01 within neurology are:

- reduction of the incidence of delayed cerebral ischaemia following subarachnoid haemorrhage; and
- multiple sclerosis (relapsing-remitting and progressive forms).

Metastatic ER+ breast cancer in combination with endocrine therapy

Globally, there are over 1.5 million diagnoses of breast cancer every year and it is the biggest cause of cancer death in women. The breast cancer therapeutics market in the eight major therapeutic markets was worth US$9.2 billion in 2013. The breast cancer therapeutic market comprises hormone therapy, chemotherapy and biological treatments.

Breast cancer can be divided into four subtypes based on over-expression of hormone receptors (ER- or ER+) and/or human epidermal growth factor receptor 2 (HER2- or HER2+). Whilst HER2+ constitutes only about 20 per cent. of diagnoses, it dominates the market from a sales perspective, with sales of Roche's Herceptin (a monoclonal antibody) being in excess of US$6 billion in 2013. ER+ subtypes represent the most prevalent subtype of breast cancer (around 75 per cent. of all breast cancers), but the market for hormonal therapies for ER+ subtypes is becoming increasingly generic as drugs come off patent. However, as a benchmark of potential in-patent sales, Anastrozole (Arimidex® AstraZeneca) achieved global peak-year sales (in 2009) of US$1.9 billion following its approval for treatment of ER+ breast cancer in the advanced and adjuvant post-menopausal settings.

The Directors anticipate that SFX-01 will be aimed at metastatic ER+ breast cancer in combination with endocrine therapy.

Reduction of the incidence of delayed cerebral ischaemia following subarachnoid haemorrhage

Subarachnoid haemorrhage, a bleed on the outer cavity of the brain, is a form of haemorrhagic stroke. SAH accounts for 1 in every 20 strokes in the UK. It affects 6-7 people in every 100,000 annually and has an average fatality rate of approximately 50 per cent. Of the survivors, 46 per cent. are left with cognitive impairment as a result of early brain injury induced by a vasospasm (constriction of blood flow) which typically occurs 4-12 days after the initial bleed.

The current standard of care for patients with SAH is the generic calcium channel blocker, nimodipine. Nimodipine has been a generic for over 20 years and no significant clinical advance has been made in that time. A recent study demonstrated that nimodipine reduces the incidence of poor outcome by 40 per cent. Accordingly, the Directors believe that there is a requirement to reduce the incidence of delayed neurological brain damage through new treatments.

The global brain haemorrhage therapeutics market was valued at US$358 million in 2010 and is projected to reach US$452 million by 2018. SAH is a recognised rare disease with the potential for orphan designation. This designation could represent an accelerated path to market. If SFX-01 is successfully demonstrated to be a treatment for SAH, the Board would consider applications in the traumatic brain injury (''TBI'') therapeutics market. The TBI market was worth US$1.5 billion in 2010 and is expected to reach US$2 billion in 2017.

Multiple sclerosis

The multiple sclerosis market in the US, Japan and five major EU markets is currently valued at US$12 billion and sales are expected to reach US$18.3 billion in 2018. This increase is largely due to the emergence of novel oral therapies (such as Novartis' Gilenya, Genzyme's Aubagio and Biogen IDEC's Tecfidera).

Tecfidera has become an important multiple sclerosis therapy with annualised sales of US$2.9 billion reported in 2014. However, following the IPO in the US of Forward Pharma, a company which aims to challenge Biogen IDEC's patent position, and concerns over the tolerability of the drug, the future market share of Tecfidera is difficult to predict. SFX-01 and Tecfidera share a common molecular target, Nrf2, and the Directors believe that if SFX-01 can be demonstrated to have clinical efficacy equal to, or in excess of Tecfidera, then it will be extremely competitive, due to Tecfidera's side effects that include GI irritation and hot flushes.

Other potential applications

Whilst prostate cancer remains a major market opportunity, the Directors have taken the decision to defer development in this area.

Whilst the Group is currently focused in the field of oncology and neurology, preclinical animal model data generated in collaborations with research establishments (under material transfer agreements) has confirmed efficacy in other major diseases, most notably osteoarthritis which is a therapeutic market worth in excess of US$5 billion globally. Furthermore, in a recently publicised placebo-controlled, double blind randomised trial (conducted by Massachusetts General Hospital for Children, the University of Massachusetts and The John Hopkins University School of Medicine), sulforaphane (administered in the form of a frozen botanical extract) has been shown to significantly improve social interaction, abnormal behaviour and verbal communication in young men with autism spectrum disorder; a therapeutics market in excess of US$1 billion globally. Although this trial was not connected to Evgen and it did not use a pharmaceutical product, the Directors believe that such clinical trials are testament to the therapeutic potential of sulforaphane and the future potential clinical demand to access and trial SFX-01 in indications outside of the Group's core target markets.

Intellectual Property

The Group's patents and patent application assets have been independently reviewed in the Patent Attorney's Report set out in Part IV of this document.

The Group works with its patent attorney, HGF, to manage its patent portfolio, and the Group's management regularly meets with a specialist intellectual property consultant to identify and prepare invention disclosures, agree patent prosecution strategy and consider questions regarding freedom to operate in respect of the Group's activities.

The Group, CSIC and University of Seville's patent and patent application portfolio constitutes:

- composition of matter in the form of a sulforaphane-cyclodextrin complex (entitled ''Stabilized sulforaphane'');
- manufacturing of sulforaphane and sulforaphane-cyclodextrin complex in the form of a scalable process (entitled ''Methods of synthesising sulforaphane'');
- methods of isolation and purification of sulforaphane (entitled ''Isolation and purification of sulforaphane''); and
- composition of matter in the form of novel analogues derived from the sulforaphane structure (entitled ''Sulforaphane derivatives'').

Major patent families protecting the Group's assets

Patent family	Patent applicant	Progress	Geography	Patent expiry
Stabilized sulforaphane	PharmAgra/Lalilab	Granted	Australia Canada USA	2028
Stabilized sulforaphane	PharmAgra/Lalilab	Filed	Europe Japan Hong Kong	2028
Methods of synthesising sulforaphane	PharmAgra/Lalilab	Filed	Australia Brazil Canada China Europe India Japan USA	2033
Isolation and purification of sulforaphane	PharmAgra/Lalilab	Filed	China Europe Japan USA	2033

Patent families held under an exclusive worldwide option agreement

Patent family	Patent applicant	Progress	Geography	Patent expiry
Sulforaphane derivatives	CSIC/Univ. Seville	Filed	Australia Canada China Europe Japan USA	2033
Sulforaphane derivatives	CSIC/Univ. Seville	Granted	Spain	2032

The patents and applications in the name of PharmAgra and Lalilab are licensed on a worldwide and exclusive basis to Evgen, with the exception of topical (for example skin) applications. Upon the recruitment of the first 50 patients into clinical trials, this patent estate and related know-how will be assigned to the Group. The Company expects to meet this milestone in 2016.

The Group also has invention records, that have not yet been filed as patent applications, relating to new use and product formulation. These will be filed as applications by the Group at the appropriate time in the clinical development process.

The Group has registered Sulforadex® as a trademark in the UK, European Union and United States.

Competition

The competition can be viewed from the perspective of the technology that has enabled the stabilisation of sulforaphane (''technology competition'') and the therapeutic market for which a future product may be approved (''product competition''). The Directors also consider it appropriate to address any potential impact of non-pharmaceutical products (''substitute competition''), given the botanical heritage of the active pharmaceutical principle.

Technology Competition

The Directors are not aware of any alternative synthetic sulforaphane-based (stabilised or otherwise) development products in the clinic. The Directors believe that all registered clinical trials (by third parties) that claim to administer sulforaphane actually administer botanical extracts that contain either (a) the sulforaphane precursor, glucoraphanin, or (b) enzymatically-treated glucoraphanin, to release sulforaphane, which is then subsequently frozen (or in one case refrigerated) prior to administration in the clinic. The Directors believe that the registered clinical trials being conducted on botanical extracts are not being executed as part of a clinical development programme to obtain marketing approval for a pharmaceutical product.

Product Competition

The Directors believe that in the ER+ metastatic breast cancer market, there are currently three agents that have a licence for co-administration with endocrine therapy. Two of these, trastuzumab and lapatinib, are licenced for the 10 per cent. of metastatic breast cancers that co-express HER2, and are therefore less relevant to the Group, as it intends to focus on the larger HER2- breast cancer market. The third agent, everolimus, is an mTORC-1 inhibitor which is licenced in combination with the steroidal aromatase inhibitor, exemestane. This combination has been shown to increase progression-free survival, but not overall survival, and resulted in a marked increase in multiple toxicities.

The Directors believe the only approved products for subarachnoid haemorrhage are based upon the generic nimodipine. The Directors are aware that improved delivery formats of nimodipine are in clinical trials. SFX-01 is intended to be administered in combination with nimodipine in the first instance.

The Directors believe that in relapsing-remitting multiple sclerosis, Biogen IDEC's Tecfidera will be the competitive standard if SFX-01 is advanced into clinical trials for this indication. It is known that SFX-01 and Tecfidera both modulate drug target, Nrf2. Tecfidera has side effects including hot flushes and GI irritation.

Substitute Competition

Since the anti-cancer activity of sulforaphane was first identified in 1992, there has been an increasing interest in general health products relating to broccoli and other brassica vegetables. There are a number of niche dietary supplement brands based on botanical extracts. These products typically contain the natural sulforaphane precursor, glucoraphanin, and the amount of sulforaphane that the human body is able to derive from these botanical extracts is limited by (a) the concentration of glucoraphanin in the product, typically 10 per cent. by dry weight, and (b) the extent to which an individual's gut flora can convert it to sulforaphane, which can vary from about 1 per cent. to more than 40 per cent. of the dose. The Directors believe that such products do not contain any significant level of sulforaphane, nor can they provide the capacity to derive standard doses of sulforaphane by the metabolism of its glucoraphanin.

The Directors are aware of only one product that claims to contain sulforaphane. The product, marketed as Prostaphane, is positioned as a dietary supplement and not a pharmaceutical. The sulforaphane content of the product is understood to be extracted from botanical sources (specifically broccoli seeds) and claims to contain 10mg sulforaphane; one-tenth of the proposed daily dose of SFX-01 in the clinical trials planned for 2016. The product is unstable at ambient temperature and is stored and distributed in refrigerator channels to a small number of French independent chemists. The Directors believe that the relatively high cost of goods, the restrictive contraints of EU Novel Food legislation, the low dose, the requirement for chilled storage and the lack of regulatory approval as a medicine render Prostaphane a niche product and not a competitive threat to a pharmaceutical product with marketing approval.

There is a long history of pharmaceuticals based upon botanical extracts. The Directors consider that non-pharmaceutical products based on botanical extracts (presented as dietary supplements) do not erode the prescription markets where patients have real clinical need and require proven efficacious medicines.

The Regulatory Environment

All pharmaceutical products are governed by stringent regulations and guidelines that dictate the type and extent of the research and development programme that needs to be conducted to demonstrate that a product is safe and effective and can be produced to the required quality each time it is manufactured. SFX-01 is currently manufactured for the Group's preclinical and clinical trials under contract by PharmAgra (also the licensor) in the United States. PharmAgra has an FDA-approved cGMP compliant manufacturing capability. The Group recognises the importance of the regulatory process and to this end retains specialist consultants to advise on regulatory strategy and operational matters.

Financial Information

The Company became the new parent company of Evgen on 5 December 2014 as part of a restructuring of the Group in preparation for Admission. The following financial information for the Group for the three years ended 31 March 2015 has been derived from the financial information contained in Part III of this document, prepared in accordance with IFRS, and should be read in conjunction with the full text of this document. Investors should not rely solely on the summarised information.

	Year ended 31 March		
	2013	**2014**	**2015**
	£'000	**£'000**	**£'000**
Loss from operations	(947)	(1,040)	(1,246)
Loss for the year	(866)	(1,077)	(2,273)

Current Trading and Prospects

Trading of the Group since 31 March 2015 continues to be in line with the Directors' expectations. The potential of the Group's technology enables the Directors to view the future with confidence and they look forward, post-Admission, to having the funds available with which to exploit the addressable markets.

The Group completed a private Pre-IPO Round raising £2 million in August 2015. On 1 September 2015, it issued a formal notice to the University of Seville and CSIC to exercise the Group's option

to negotiate a world-wide licence for a range of novel sulforaphane analogues, thereby building its preclinical pipeline behind the lead clinical development product, SFX-01.

Details of the Placing

Pursuant to the Placing Agreement, Northland Capital has agreed conditionally to use its reasonable endeavours to find subscribers for 18,918,919 New Ordinary Shares (representing 26 per cent. of the Enlarged Share Capital) at the Placing Price. The issue of New Ordinary Shares will raise gross proceeds of approximately £7 million for the Company (approximately £6.3 million net of all expenses).

The Placing, which is not underwritten, is subject to the satisfaction of conditions set out in the Placing Agreement, including there being no breach of the warranties set out in the Placing Agreement prior to Admission and Admission occurring on or before 8.00 a.m. on 21 October 2015 (or such later time and/or date as may be agreed between Northland Capital and the Company, being not later than 6 November 2015). The Placing Agreement contains a provision entitling Northland Capital to terminate the Placing at any time prior to Admission in certain circumstances.

The Placing Shares will be issued credited as fully paid and will on issue rank *pari passu* in all respects with each other and the Existing Ordinary Shares and will rank in full for all dividends and other distributions thereafter declared, made or paid on the ordinary share capital of the Company. Upon Admission the Ordinary Shares will be freely transferable.

Further details of the terms of the Placing Agreement are set out in paragraph 10.5 of Part VI of this document.

Use of Proceeds

The net proceeds of the Placing will be used as follows:-

- to fund a Phase IIa clinical trial on SFX-01 in metastatic breast cancer; £1.8 million
- to enhance and accelerate a Phase II clinical trial on SFX-01 in subarachnoid haemorrhage; £0.7 million
- to fund long-term safety and toxicology studies on SFX-01; £0.6 million
- to fund preclinical studies on SFX-01 in models of multiple sclerosis; £0.4 million
- to fund an assessment and early preclinical development of novel sulforaphane analogues; £0.4 million
- to expand existing, or initiate new, preclinical or clinical work programmes as deemed appropriate by the Board; and £1.2 million
- for working capital purposes (including IP costs and licence fees) £1.2 million

Lock-in and Orderly Market Arrangements

Each of the Directors and certain Shareholders have agreed, subject to certain limited exceptions, not to dispose of their interests in, in aggregate, 39.5 million Ordinary Shares for a period of 12 months from Admission. Certain Shareholders have agreed with the Company and Northland Capital not to dispose of, in aggregate, 7.2 million Ordinary Shares owned by them for a period of 12 months from Admission, subject to certain limited exceptions, including should the Company's volume weighted average share price exceed 200% of the Placing Price for a period of 20 consecutive business days during the 12 month period following Admission. All of these Shareholders have also agreed to certain orderly market provisions for a further twelve months up to the second anniversary of the date of Admission, whereby they agree to only deal in their Ordinary Shares through Northland Capital (or such other reputable broker as appointed by the Company from time to time) or, in the event that Northland Capital (or such other reputable broker as appointed by the Company from time to time) cannot place the relevant number of shares at the requested price, through a third party broker at a higher price and on terms no less favourable than those offered by Northland Capital (or such other reputable broker as appointed by the Company from time to time).

In addition to the hard lock-ins described above, certain other existing Shareholders have agreed not to dispose of their interests in, in aggregate, 3.4 million Ordinary Shares for a period of between six to twelve months following Admission, other than through Northland Capital, subject to limited exceptions.

Further details of the terms of the hard lock-in, soft lock-in and orderly market arrangements are set out in paragraphs 10.5, 10.6 and 10.7 of Part VI of this document.

Directors, Senior Management and Employees

Barry Clare, Executive Chairman, aged 62

Barry is an experienced healthcare company director who joined Evgen as Chairman in 2009. Having graduated in Natural Sciences at Cambridge University, Barry joined Procter & Gamble where he spent 10 years working in a variety of product development roles in the UK and in Europe. In 1984, he joined Diversey Corporation, the speciality chemicals division of Molson Companies, as corporate Vice President and VP Marketing in Canada where he led its transformation from a commodity chemical supplier to a leading differentiated business solutions provider to the food and hospitality industries. In 1991, Barry joined Boots Company plc as managing director of Boots Healthcare International, the company's over-the-counter ("OTC") consumer healthcare division. Between 1991 and 2001, the business became the fastest growing OTC company in Europe and included the global expansion of brands such as Nurofen, Strepsils and Clearasil. In 1999, he was appointed to the board of Boots Company plc and became managing director of Boots Retail International. He was appointed group marketing director of Boots Company plc in 2002, a position he held until 2003 when he left to set up Clarat Partners LLP, a specialist firm to participate in transactions in the healthcare, medical devices, beauty, personal care and well-being sectors. Barry, who served as a non-executive director of Standard Chartered plc between 2001 and 2003, is on the board of several private healthcare companies and is non-executive chairman of University Hospital of South Manchester Foundation Trust. Barry has been a Director and Chairman of Evgen since November 2009.

It is intended that Barry will serve as Executive Chairman of Evgen Pharma for approximately one year from Admission, following which he will become non-executive Chairman of Evgen Pharma.

Dr Stephen ("Steve") Franklin, Chief Executive Officer, aged 47

Steve, the founder of Evgen, has over 20 years' commercial experience in life science industries, focusing on the commercialisation of new technology. He was the CEO of Provexis plc, a nutraceutical company, and led that company through its admission to AIM in 2005. Prior to that, Steve was a principal executive with ANGLE plc, the AIM quoted technology commercialisation company, having previously held a business development role with Manchester Biotech (now University of Manchester Innovation Company), one of the largest campus-based incubators in Europe. In these roles, he helped establish a portfolio of drug discovery and development businesses. Steve has a BSc in Biology (York), a PhD in Applied Biochemistry (Nottingham) and an MBA with distinction (Nottingham). He is a Fellow of the Royal Society of Medicine and an alumnus of the Royal Commission for the Exhibition of 1851. Since founding Evgen in 2008, Steve has raised a total of £6.2 million in funding for the Group, successfully in-licensed technologies, taken SFX-01 through preclinical safety and toxicology and subsequent Phase I trials, and has established collaborations with research institutes in the UK, USA and Spain.

John Bradshaw, Finance Director, aged 51

John is a qualified chartered accountant with over 20 years' post-qualification experience working as a finance director for UK quoted and venture capital owned companies. John trained with Arthur Andersen, where he worked from 1986 until 1997, when he joined Gyrus Group plc as finance director ahead of its flotation on the Official List. Since leaving Gyrus in 2001, John acted as finance director for Analysys Limited, TeraView Limited and HCEG plc and since 2006 has provided interim and part time finance director services to start-up and other venture capital funded companies, since 2012 through Bradshaw Daniel Limited. John is also a non-executive director of Ixico plc, where he serves as Chairman of the Audit Committee. John became a director of Evgen Pharma in November 2014.

Dr Susan Foden, Non-executive Director, aged 62

Susan has an MA, D.Phil in biochemistry from the University of Oxford. Susan held research appointments at AEA Technology, Harwell, before joining Celltech plc in 1983 where she became head of academic liaison. In 1987, Susan was appointed Chief Executive of Cancer Research Campaign Technology Ltd ("CRCT") establishing the company and building its operations to one with significant royalty streams and equity in spin-out companies. From 1998 to 2000, she was also Chief Executive of Cancer Research Ventures Ltd, a subsidiary of CRCT, set up to transfer

cancer technologies outside the Cancer Research Campaign portfolio in the UK and overseas. In 2000, Susan joined Merlin Biosciences Ltd where she was an investor director with a focus on healthcare until 2003. Susan holds various non-executive directorships including BTG plc and Vectura Group plc and is the non-executive chair of BerGenBio AS. She is a member of the investment Committee for CD3, a joint initiative between the University of Leuven and the European Investment Fund. Susan was appointed as a non-executive director of Evgen in 2011 and became a director of Evgen Pharma in November 2014.

Dr Mark Wyatt, Non-executive Director, aged 43

Mark is currently an Investment Director at Enterprise Ventures where he has a particular focus on investments in the life sciences sector. He has over 15 years' experience working in venture capital and has previously held senior positions at Merlin Biosciences and Imperial Innovations, both specialist life science investors. He has board level experience in both private and public companies. Mark has a PhD from the Glaxo Institute of Applied Pharmacology at Cambridge University, and is a Sainsbury's Management Fellow in Life Sciences, receiving an MBA from Warwick. Mark was appointed a non-executive director of Evgen in June 2012 and became a director of Evgen Pharma in November 2014.

Dr Marc d'Abbadie, Non-executive Director, aged 37

Marc is an Investor Director at SPARK Impact, the manager of the North West Fund for Biomedical. NWFB first invested in Evgen in 2011. Marc has represented NWFB Directors Limited, a corporate director of Evgen since 2011. Marc was previously at Inventages, which manages one of the world's largest life science focused venture capital funds with assets of US$1.5bn; at Technikos, a medical device venture capital investor; and was also a consultant at McKinsey & Co. He has published in peer-reviewed scientific journals, is a named inventor on two patents and had founded a start-up. Marc obtained his MA in Natural Sciences from Trinity College and his PhD in Biochemistry from the MRC Laboratory of Molecular Biology, both at the University of Cambridge. Marc became a director of Evgen Pharma in his own name in November 2014.

Dr Alan Barge, Non-executive Director, aged 58

Alan has held high-level strategic leadership roles in oncology with global pharmaceutical companies. He is currently Chief Medical Officer of Singapore-based ASLAN Pharmaceuticals PTE. He was the Clinical Vice President and Head of Oncology & Infection at AstraZeneca where he was directly responsible for the company's overall strategy in oncology and infection, from drug discovery to proof-of-concept. He was also the Head of the Therapy Area Portfolio Team and accountable for the design and delivery of all projects and budgetary accountability of approximately US$200 million per annum at AstraZeneca. Prior to this, Alan held other positions in AstraZeneca, including Clinical Vice President (Oncology & Infection), Worldwide Medical Director (Iressa), and Global Product Director (Emerging Oncology). Prior to his career at AstraZeneca, Alan was European Medical Director for Amgen Inc. Alan will become a director of Evgen Pharma immediately before Admission.

Senior management

Dr David Howat, Chief Development Officer, aged 56

David has over 20 years' experience in pharmaceutical industry R&D. He became the Group's Chief Development Officer in 2011. From 2003 to 2011, he was a freelance preclinical development and project management consultant and, in this role, was responsible for the establishment of the development infrastructure, project plans, establishment of contracts for manufacturing, analysis, safety, assessment and the Phase I regulatory filings for a number of small drug development companies. Prior to 2003, David was Head of Project Management for KS Biomedix Holdings, a biopharmaceutical company developing a pipeline of drugs for a range of cancer indications. Prior to KS Biomedix Holdings, he was the Director of Preclinical Development for NicOx SA and was a Team Leader at Celltech Chiroscience.

Employees

The Group currently has two full-time employees, three part-time employees and four consultants. The average monthly number of employees (including executive and Non-executive Directors) for the last three financial years was as follows:

	2013 Number	2014 Number	2015 Number
Administration	1	1	1
Executive and Non-executive Directors	6	6	6
	7	7	7

Corporate Governance

The Directors recognise the importance of sound corporate governance and confirm that, following Admission, they intend to comply, so far as practicable and to the extent appropriate for a company of its nature and size, with the recommendations in the QCA Code, which have become a widely recognised benchmark for corporate governance of smaller quoted companies, particularly AIM companies.

Following Admission, the Board will meet around ten times a year to review, formulate and approve the Group's strategy, budgets, corporate actions and oversee the Group's progress towards its goals. There are Audit and Remuneration Committees in place with formally delegated duties and responsibilities and with specific terms of reference. From time to time separate committees may be set up by the Board to consider specific issues when the need arises. Susan Foden has been appointed as the Senior Independent Director. Due to the size of the Group, the Directors have decided that issues concerning the nomination of directors will be dealt with by the Board rather than a committee but will regularly reconsider whether a nominations committee is required.

The Group has both an Audit and a Remuneration committee with formally delegated duties and responsibilities. The Audit Committee comprises Marc d'Abbadie as Chair, Susan Foden and Alan Barge. The Remuneration Committee comprises Susan Foden as Chair, Mark Wyatt and Alan Barge.

The Audit Committee determines the terms of engagement of the Group's auditors and will determine, in consultation with the auditors, the scope of the audit. The Audit Committee receives and reviews reports from management and the Group's auditors relating to the interim and annual accounts and the accounting and internal control systems in use throughout the Group. The Audit Committee has unrestricted access to the Group's auditors.

The Remuneration Committee reviews the scale and structure of the Executive Directors' and senior employees' remuneration and the terms of their service or employment contracts, including share option schemes and other bonus arrangements. The remuneration and terms and conditions of the Non-executive Directors are set by the entire Board.

Following Admission, the Board will be responsible for monitoring the Group's risks and implementing other systems which are deemed necessary.

Share Option Schemes

The Board recognises the importance of ensuring that employees of the Group are effectively and appropriately incentivised and their interests aligned with those of the Group. The Board regards employee share ownership as a key part of such incentive arrangements.

The Group has granted unapproved options to employees and directors of the Group under the 2008 Scheme and by way of Standalone Unapproved Agreements and has granted tax favoured EMI options under the 2011 Plan. There are 6,991,200 Ordinary Shares under option at the date of this document, representing 9.6 per cent. of the enlarged share capital of the Company. All of the options granted under the 2008 Plan, the 2011 Plan and by way of Standalone Unapproved Agreements will become fully vested and exercisable on Admission.

The Company has adopted the LTIP and DBP and granted the LTIP IPO Awards, in each case conditional upon Admission. There are 1,754,051 Ordinary Shares the subject of the LTIP IPO Awards.

All awards granted under the LTIP, the DBP or any other employees' share scheme operated by the Company are subject to a limit that in any period of ten calendar years, not more than 10 per cent. of the Company's issued ordinary share capital may be issued under any such plan or scheme. Options granted on or before Admission and the LTIP IPO Awards do not count towards this limit.

Further details of the Company's incentivisation arrangements are set out in paragraph 12 of Part VI of this document.

Warrants

Following Admission, there will be 1,457,418 outstanding Warrants to subscribe for 1,457,418 Ordinary Shares at the Placing Price of 37p per Ordinary Share. Further details on the Warrants are set out in paragraph 10.8 of Part VI of this document.

Dividend Policy

The Company is primarily seeking to achieve capital growth for its Shareholders. It is the Board's intention during the current phase of the Group's development to retain future distributable profits from the business, to the extent any are generated. The Directors do not anticipate declaring any dividends in the foreseeable future.

Taxation

Your attention is drawn to the United Kingdom Taxation section contained in paragraph 17 of Part VI of this document. If you are in any doubt as to your tax position, you should consult your own independent financial adviser immediately.

EIS and VCT Status

The Company has received advance assurance from HMRC that the New Ordinary Shares to be issued pursuant to the Placing will rank as ''eligible shares'' for the purposes of EIS and will be capable of being a ''qualifying holding'' for the purposes of investment by VCTs, however, none of the Company, the Directors or any of the Company's advisers give any warranty or undertaking that such reliefs will continue to be available and not withdrawn at a later date.

The Directors consider that the Company or its subsidiaries have received, in the 12 months immediately prior to the Placing, investments totalling £2,150,104 (including under EIS and from VCTs) pursuant to a measure approved by the European Commission as compatible with Article 107 of the Treaty on the Functioning of the European Union in accordance with the principles laid down in the European Commission's Guidelines on State aid to promote risk finance investments. Accordingly, the Placing will limit funds up to £2,800,000 from VCTs, investors seeking EIS reliefs and any other State aid risk capital investors in order not to exceed the maximum amount of £5 million that can be raised annually through risk capital schemes.

The Summer Finance Bill 2015 proposes a lifetime limit of risk finance investments (which include those from VCTs and under the EIS) of £12 million or £20 million for a knowledge intensive company (which the Directors consider the Company would be). The Group has raised prior to the Placing a total amount of £2,446,541 of such risk finance and therefore, with any such further risk finance in the Placing, the Company and its Group would be below these proposed lifetime limits.

Immediately prior to the Placing, all of the 2013 Loan Notes will convert into A Shares and all of the 2014 Loan Notes will convert into Ordinary Shares. The A Shares will convert into Ordinary Shares at Admission in accordance with the Existing Articles, as further described in paragraph 4.8.7 of Part VI of this document. Holders of Loan Notes who subscribed for shares in the capital of Evgen or, following 5 December 2014, Evgen Pharma and who sought EIS relief after 21 October 2012 and subsequently subscribed for Loan Notes may have some or all of any EIS relief attributable to such shares reduced or withdrawn as a result of such a conversion. Any person who is in any doubt about their tax position should consult their own professional adviser.

Share Dealing Code

With effect from Admission, the Company will adopt a share dealing code which is appropriate for a company whose shares are admitted to trading on AIM (particularly relating to dealing during close periods in accordance with Rule 21 of the AIM Rules for companies) to regulate dealings in

the Ordinary Shares by Directors and any other applicable employees (as defined by the AIM Rules for Companies).

Admission, Settlement and Dealing

Admission is expected to take place, and dealings in the Ordinary Shares are expected to commence on AIM, at 8.00 am on 21 October 2015. These dates and times may change.

CREST is a paperless settlement procedure enabling securities to be evidenced otherwise than by a certificate and transferred otherwise than by a written instrument. The Articles permit the holding of Ordinary Shares under the CREST system. The Existing Ordinary Shares are admitted to CREST and the Company has applied for the New Ordinary Shares to be admitted to CREST with effect from Admission. Accordingly, settlement of transactions in all Ordinary Shares held in uncertificated form following Admission will take place within the CREST system.

CREST is a voluntary system and holders of Ordinary Shares who wish to receive and retain share certificates will be able to do so.

All Placing Shares will be issued payable in full at the Placing Price. It is intended that, if applicable, definitive share certificates in respect of the Placing Shares will be distributed by 28 October 2015 or as soon thereafter as is practicable. No temporary documents of title will be issued.

Risk Factors

The Group's business is dependent on many factors and prospective investors should read the whole of this document, in particular, your attention is drawn to the risk factors set out in Part II of this document.

Further Information

Your attention is drawn to the additional information set out in Parts II to VI of this document.

PART II

RISK FACTORS

There are significant risks associated with the Company. Prior to making an investment decision in respect of the Ordinary Shares, prospective investors should consider carefully all of the information within this document, including the following risk factors. The Directors believe the following risks to be the most significant for potential investors. However, the risks listed do not necessarily comprise all those associated with an investment in the Company. In particular, the Company's performance may be affected by changes in market or economic conditions and in legal, regulatory and/or tax requirements. The risks listed are not set out in any particular order of priority. Additionally, there may be risks not mentioned in this document of which the Directors are not aware or believe to be immaterial but which may, in the future, adversely affect the Company's business and the market price of the Ordinary Shares.

If any of the following risks were to materialise, the Group's business, financial condition, results or future operations could be materially and adversely affected. In such cases, the market price of the Ordinary Shares could decline and an investor may lose part or all of his investment. Additional risks and uncertainties not presently known to the Directors, or which the Directors currently deem immaterial, may also have an adverse effect upon the Company and the information set out below does not purport to be an exhaustive summary of the risks affecting the Company.

Before making a final investment decision, prospective investors should consider carefully whether an investment in the Company is suitable for them and, if they are in any doubt should consult with an independent financial adviser authorised under FSMA which specialises in advising on the acquisition of shares and other securities.

RISKS RELATING TO THE GROUP'S BUSINESS

Dependence on key personnel

The success of the Group, in common with other businesses of a similar size, will be highly dependent on the expertise and experience of the Directors and senior management. However, the retention of such key personnel cannot be guaranteed. Should key personnel leave, the Group's business, prospects, financial condition or results of operations may be materially adversely affected.

Early stage of operations

Evgen Pharma's operations are at an early stage of development and there can be no guarantee that the Group will be able to, or that it will be commercially advantageous for the Group to, develop its proprietary technology. Further, the Group has no positive operating cash flow and does not expect to generate any revenue until 2018 at the earliest. The Group's ultimate success will depend on the Directors' ability to implement the Group's strategy, generate cash flow and access equity markets. Whilst the Directors are optimistic about the Group's prospects, there is no certainty that anticipated outcomes and sustainable revenue streams will be achieved. The Group will not generate any material income until commercialisation of its proprietary technology has successfully commenced. The Group has sustained losses in each year since Evgen commenced operations in 2008.

The Group expects to continue to incur substantial expenditure in order to develop its business and, based on the amount of this expenditure it expects to continue to expend its cash reserves for some time. Prior losses, combined with expected future losses, have had and may continue to have an adverse effect on shareholders' equity and working capital. Moreover, the net losses the Group incurs may fluctuate significantly from year to year, such that a period-to-period comparison of results of operations may not be a good indication of future performance. The amount of the Group's future net losses will depend, in part, on the rate of its future expenditure and its ability to obtain funding through equity financings or strategic collaborations. The quantum of net losses will also depend on the Group's success in developing and commercialising its proprietary technology in order to generate revenue and become profitable. The Group's failure to become and remain profitable would depress the value of the Ordinary Shares and could impair its ability to raise further equity capital, expand its business, maintain its research and development efforts, diversify

its product offerings or even continue its operations. There can be no assurance that the Group's proposed operations will be profitable or produce a reasonable return, if any, on investment.

The Group has not demonstrated its ability to obtain regulatory approvals or conduct sales and marketing activities necessary for successful product commercialisation. In addition, given its limited operating history, the Group may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors.

Technology and products

Evgen Pharma is a drug development company. The development and commercialisation of its proprietary technology, which is at an early stage, will require multiple series of clinical trials and there is a risk that safety issues may arise when the product is tested. Serious unforeseen side effects from the development product could arise, either during clinical development or, if approved by regulatory authorities, after the approved product has been marketed. The results of future clinical studies may show that the Group's development products cause undesirable or unacceptable side effects, or that the development product lacks the necessary level of efficacy to obtain a regulatory approval. Any of these factors could interrupt, delay or halt clinical studies and result in the delay of, or failure to obtain, marketing approval from the regulatory authorities, or result in marketing approval with restrictive label warnings or potential product liability claims. Moreover, as larger numbers of subjects are enrolled in advanced clinical studies for the Group's development product or if the Group's development product receives marketing approval, the risk that uncommon or low frequency but significant side effects are identified may increase. If the Group's development product receives marketing approval, and the Group or others subsequently identify undesirable or unacceptable side effects caused by such products:

- regulatory authorities may require the Group to take its approved product off the market;
- regulatory authorities may require the addition of labelling statements, specific warnings, a contraindication or field alerts to physicians and pharmacies;
- the Group may be required to change the way the product is administered, conduct additional clinical studies or change the labelling of the product;
- the Group may be subject to limitations on how it may promote the product;
- sales of the product may decrease significantly;
- the Group may be subject to litigation or product liability claims; and
- the Group's reputation may suffer.

Any of these events could prevent the Group or any potential future partners from achieving or maintaining market acceptance of the affected product, or could substantially increase commercialisation costs and expenses, which in turn could delay or prevent the Group from generating significant revenue from the sale of its product.

Product development timelines are at risk of delay, particularly since it is not always possible to predict the rate of patient recruitment into clinical trials. There is a risk therefore that product development could take longer than presently expected by the Directors. If such delays occur, the Group may require further working capital.

Failure of a clinical trial may occur at any stage of the testing, and the Group may experience numerous unforeseen events during, or as a result of, the clinical study process that could delay or prevent commercialisation of its development product. Several factors could result in the failure or delay in completion of a clinical study including, but not limited to:

- delays in securing clinical investigators or clinical study sites;
- delays in obtaining institutional review board, ethics committee or other regulatory approvals to commence a clinical study;
- the inability to monitor subjects adequately during or after treatment, or problems with the investigator or subject compliance with the study protocols;
- the inability or unwillingness of medical investigators to follow agreed-upon clinical protocols;
- unexpected adverse events or other safety issues; and
- absence of any observed clinical benefit.

The time required for regulatory review varies from country to country and can be lengthy, expensive and uncertain. While efforts will be made to ensure compliance with government

standards, there is no guarantee that the Group's products will be able to achieve the necessary regulatory approvals to enable the Group to promote its products in any of the targeted markets and any such regulatory approval may include significant restrictions for which the Group's products can be used.

In addition, the Group may be required to incur significant costs in obtaining or maintaining its regulatory approvals. Delays or failure in obtaining regulatory approval would be likely to have a serious adverse effect on the value of the Group and have a consequent impact on its financial performance. If the Group does not obtain regulatory approval to commercialise a development product, or if such approval is delayed, the Group's business, results of operation and/or financial condition could be materially adversely affected.

Safety, toxicity or efficacy issues with one of the Group's development products in one indication may negatively impact the viability of that development product in another indication.

There is no guarantee that the clinical trials will demonstrate efficacy in patients. When healthy volunteers were dosed with SFX-01 for just 7 days as part of the Phase I trial, no statistical change was noted in levels of HDAC; although movement of this biomarker would not necessarily be expected in healthy subjects, or indeed in patient groups after just 7 days' dosing.

Dependence on Third Parties

The Group outsources certain functions, tests and services to contract research organisations, medical institutions and other specialist providers, and the Group relies on these third parties for quality assurance, clinical monitoring, clinical data management and regulatory expertise. The Group has engaged, and may in the future engage, a CRO to run all aspects of a clinical study on its behalf. There is no assurance that such individuals or organisations will be able to provide the functions, tests or services as agreed upon or in quality fashion and the Group could suffer significant delays in the development of its development product.

The Group does not currently have, nor does it plan to acquire, the infrastructure or capability internally to manufacture its development product for use in the conduct of its clinical studies, or to manufacture its product. The Group does not control the manufacturing processes of the third parties it contracts with and is dependent on those third parties for the production of its development product in accordance with relevant regulations, which includes, among other things, quality control, quality assurance and the maintenance of records and documentation.

If the Group were to experience an unexpected loss of supply of, or if any supplier were unable to meet its demand for, a development product, it could experience delays in its research or planned clinical studies or commercialisation. The Group may be unable to find alternative suppliers of acceptable quality, in the appropriate volumes at an acceptable cost.

If the Group enters into arrangements with third parties to perform development, sales and marketing services, the Group's product revenues could be lower than if the Group were to develop, market and sell the product itself. In addition, the Group may not be successful in entering into arrangements with third parties to sell and market its products or may be unable to do so on terms that are favourable to the Group. Acceptable third parties may fail to devote the necessary resources and attention to sell and market the Group's product effectively. If the Group does not establish development, sales and marketing capabilities successfully, either on its own or in collaboration with third parties, it will not be successful in commercialising its product, which in turn would have a material adverse effect on its business, prospects, financial condition and results of operation.

Collaboration

The Group does not have sales or marketing infrastructure and has no experience in the sale or marketing of a pharmaceutical product. The Group may seek to collaborate with pharmaceutical and biotechnology companies for the development and potential commercialisation of the development products. The Group may face significant competition as well as risks in seeking and maintaining appropriate collaborations. Any collaboration agreement into which the Group may enter may call for the licensing or cross-licensing of potentially blocking patents, know-how or other intellectual property. Due to the potential overlap of data, know-how and IP, there can be no assurance that one of the Group's collaborators will not dispute its right to use, license or distribute such data, know-how or other IP, and this may potentially lead to disputes, liability or termination of the collaboration.

In addition, the Group may also be restricted under future licence agreements from entering into agreements on certain terms with potential collaborators. Should the Group seek to enter into collaboration agreements, but not be able to negotiate the terms of such agreements on a timely basis, on acceptable terms, or at all, it may have to curtail or delay the progression of a development product or programme. This would delay the Group's potential commercialisation of the development product or reduce the scope of any sales or marketing activities, increase its expenditure to develop and commercialise its development product and could materially adversely affect its business, prospects, financial condition and results of operation.

Competition

Technological competition from pharmaceutical companies, biotechnology companies and universities is intense and can be expected to increase, as well as competition from non-pharmaceutical alternative therapies. Many competitors and potential competitors of the Group have substantially greater product development capabilities and financial, scientific, marketing and human resources than the Group. The future success of the Group depends, in part, on its ability to maintain a competitive position, including an ability to further progress through the necessary clinical trials towards regulatory approval for sale and commercialisation. Other companies may succeed in commercialising their products earlier than the Group or may develop a product that is more effective than that which is produced by the Group. While the Group will seek to develop its capabilities in order to remain competitive, there can be no assurance that research and development by others will not render the Group's IP obsolete or uncompetitive.

Patents

The field of pharmaceutical development is highly litigious. The Group's priorities are to protect its IP and seek to avoid infringing other companies' IP. The Group engages reputable legal advisers to mitigate the risk of patent infringement and to assist with the protection of the Group's IP, however no guarantee can be made that infringement proceedings will not be initiated against the Group.

In respect of its own IP, the Group may face opposition from other companies to its patent applications and those applications may be the subject of third party observations. There is a risk that those observations may be successful, resulting in the Group's patent applications not proceeding to grant at all, or the claims of such being reduced in scope. Furthermore, the Group's IP is vulnerable to challenge after a patent is granted in the form of invalidity proceedings. In the event invalidity proceedings are successful, the granted patent may be revoked, or the claims of such significantly reduced in scope. If, in a particular country, any of the Group's patent applications are successfully opposed, or its patents successfully revoked, any third party may practice the invention described in the patent application or patent without infringing, and there would be serious and adverse implications for the value of the Group's IP.

As a general rule, a patent cannot be enforced until it has been granted. The Group will be unable to take action against third parties who infringe its IP unless and until a patent has been granted in the country or economic area in which the infringement has taken place.

A patent is limited territorially to the country or economic area in which it was granted. There are countries in which the Group has not filed patent applications and in those countries the invention described in any patent application filed in another country can be practiced without infringing.

Some territories have patent applications pending and not all patent applications filed by the Group have gone through the full patent prosecution process. For example, it should be noted that (i) the ''stabilization of sulforaphane'' core patent family is not yet granted in Europe, Japan and Hong Kong and (ii) the other patent families are mostly pending applications and grant cannot be guaranteed (see the Patent Attorney's Report in Part IV of this document, for an independent evaluation). Furthermore, the different approaches of patent offices in different countries may lead to patents of different scope being granted in respect of the same invention in different jurisdictions.

The Group's counterparties may become insolvent

There is a risk that the parties with whom the Group trades or has other business relationships may become insolvent. The patents protecting the technology used by the Group, including (i) the ''stabilization of sulforaphane'' core patent family owned by PharmAgra and Lalilab and (ii) the patent family owned by the Spanish National Research Council (CSIC) in collaboration with the

University of Seville are in-licensed by the Group and the Group's rights to them may be lost if the counterparty becomes insolvent or the Group materially breaches the terms of its licences. In the event that a party with whom the Group trades becomes insolvent, this could have a material adverse impact on the revenues and profitability of the Group.

Reimbursement

Government authorities and third-party payers, such as private health insurers, decide which pharmaceutical products they will cover and the amount of reimbursement. Reimbursement by a third-party payer may depend upon a number of factors, including the third-party payer's determination that use of a product is:

- a covered benefit under its health plan;
- safe, effective and medically necessary;
- appropriate for the specific patient; and
- cost-effective.

Obtaining coverage and reimbursement approval for a product from a government authority or other third-party payer is a time-consuming and costly process that could require the Group to provide to the payer supporting scientific, clinical and cost-effectiveness data for the use of its product. The Group may not be able to provide data sufficient to gain acceptance with respect to coverage and reimbursement. If reimbursement of the Group's product(s) is limited in scope or amount, or if pricing is set at unsatisfactory levels, the Group may be unable to achieve or sustain profitability.

Future funding requirements

The Company will need to raise additional funding to undertake work beyond that being funded by the net proceeds of the Placing. There is no certainty that this will be possible at all, or on acceptable terms. In addition, the terms of any such financing may be dilutive to, or otherwise adversely affect, Shareholders.

NWFB Relationship Agreement

The Group has received investments totalling £1.7 million from NWFB. It was a condition of taking this funding that the Group gave certain acknowledgements, undertakings and confirmations to NWFB regarding, amongst other things, the maintenance of its records, the provision of information, its compliance with applicable laws, regulation and guidance, its approach to capital purchases, and its co-operation in ensuring that NWFB complies with its obligations to the European Investment Bank and the European Regional Development Fund. These acknowledgements, undertakings and confirmations are currently documented in the NWFB Relationship Agreement, further details of which are set out in paragraph 10.2 of Part VI of this document.

The NWFB Relationship Agreement provides that if:

- the Company were to relocate a material part of its operations, people or trading to outside of the North West of England region;
- the investment in the Company by NWFB is deemed to be or becomes ineligible under the investment objectives and policies of NWFB (as the same may be varied from time to time at the discretion of, in particular, the European Investment Bank, the European Regional Development Fund and NWFB);
- there has been a breach of those objectives and policies; or
- the European Investment Bank, the European Regional Development Fund, NWFB or other body connected with NWFB are obliged to pay back monies which they made available to NWFB,

and NWFB so demands, then the Company must repay NWFB in such a manner and at such time as NWFB may determine, all ineligible monies which have been made available to the Group by NWFB. If NWFB were to exercise its right to demand repayment of ineligible monies, the Company may need to raise additional funding. There is no certainty that this would be possible at all, or on acceptable terms.

General legal and regulatory issues

The Group's operations are subject to laws, regulatory restrictions and certain governmental directives, recommendations and guidelines relating to, amongst other things, occupational safety, laboratory practice, the use and handling of hazardous materials, prevention of illness and injury, environmental protection and animal and human testing. There can be no assurance that future legislation will not impose further government regulation, which may adversely affect the business or financial condition of the Group.

Misconduct

The Group is exposed to the risk of employees, independent contractors, principal investigators, consultants, commercial partners or vendors engaging in fraud or other misconduct. Misconduct could include intentional failures to comply with regulations, or to provide accurate information to the regulators, or to comply with manufacturing standards the Group has established. Employee misconduct could also involve the improper use of information obtained in the course of clinical studies, which could result in regulatory sanctions and serious harm to the Group's reputation. It is not always possible to identify and deter employee misconduct, and the precautions the Group takes to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses, or in protecting the Group from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. If any such actions are instituted against the Group, and the Group is not successful in defending itself or asserting its rights, those actions could have a significant impact on its business, including the imposition of significant fines or other sanctions, and its reputation.

Computer system failure

Despite the implementation of security measures, any of the internal computer systems belonging to the Group or its third-party service providers and collaborators are vulnerable to damage from computer viruses, unauthorised access, natural disasters, terrorism, war and telecommunication and electrical failure. Any system failure, accident or security breach that causes interruptions in its own or in third-party service providers' and collaborators' operations could result in a material disruption of its product development programmes. To the extent that any disruption or security breach results in a loss or damage to its data or applications, or inappropriate disclosure of confidential or proprietary information, the Group may incur liability as a result, its product development programmes and competitive position may be adversely affected and the further development of its development products may be delayed. Furthermore, the Group may incur additional costs to remedy the damage caused by these disruptions or security breaches.

RISKS RELATING TO AN INVESTMENT IN THE ORDINARY SHARES

Trading and performance of Ordinary Shares

The AIM Rules are less demanding than those of the Official List, and an investment in a company whose shares are traded on AIM is likely to carry a higher risk than an investment in a company whose shares are quoted on the Official List. It may be more difficult for investors to realise their investment in a company whose shares are traded on AIM, than to realise an investment in a company whose shares are quoted on the Official List. The share price of publicly traded, early stage companies can be highly volatile. The price at which the Ordinary Shares will be traded and the price at which investors may realise these investments will be influenced by a large number of factors; some specific to the Group and its operations, and some which may affect quoted companies generally. The value of Ordinary Shares will be dependent upon the success of the operational activities undertaken by the Group, and prospective investors should be aware that the value of the Ordinary Shares can go down as well as up. Furthermore, there is no guarantee that the market price of an Ordinary Share will accurately reflect its underlying value.

Volatility of share price

The trading price of the Ordinary Shares may be subject to wide fluctuations in response to a number of events and factors, such as:

- variations in operating results;
- announcements of innovations or new services by the Group or its competitors;
- changes in financial estimates and recommendations by securities analysts;

- the share price performance of other companies that investors may deem comparable to the Company;
- news reports relating to trends in the Group's markets;
- large purchases or sales of Ordinary Shares;
- liquidity (or absence of liquidity) in the Ordinary Shares;
- currency fluctuations;
- legislative or regulatory changes; and
- general economic conditions.

These fluctuations may adversely affect the trading price of the Ordinary Shares, regardless of the Comapny's performance.

Future sales of Ordinary Shares could adversely affect the price of the Ordinary Shares

Certain Shareholders have given lock-in undertakings that, save in certain circumstances, they will not, until twelve months following Admission, dispose of the legal or beneficial ownership of, or any other interest in, Ordinary Shares held by them. There can be no assurance that such parties will not effect transactions upon the expiry of the lock-in or any earlier waiver of the provisions of their lock-in. The sale of a significant number of Ordinary Shares in the public market, or the perception that such sales may occur, could materially adversely affect the market price of the Ordinary Shares.

Shareholders not subject to lock-in arrangements and, following the expiry of twelve months following Admission (or earlier in the event of a waiver of the provisions of the lock-in), Shareholders who are otherwise subject to lock-in arrangements, may sell their Ordinary Shares in the public or private market and the Company may undertake a public or private offering of Ordinary Shares. The Company cannot predict what effect, if any, future sales of Ordinary Shares will have on the market price of the Ordinary Shares. If Shareholders were to sell, or the Company was to issue a substantial number of Ordinary Shares in the public market, the market price of the Ordinary Shares could be materially adversely affected. Sales by Shareholders could also make it more difficult for the Company to sell equity securities in the future at a time and price that it deems appropriate.

Dilution of Shareholders' interests as a result of additional equity fundraising

The Company may need to raise additional funds in the future to finance, amongst other things, working capital. If additional funds are raised through the issuance of new equity or equity-linked securities of the Company other than on a *pro rata* basis to existing Shareholders, the percentage ownership of the existing Shareholders may be reduced. Shareholders may also experience subsequent dilution. The Company may also issue shares as consideration shares on acquisitions or investments which would also dilute Shareholders' respective shareholdings.

Dividends

There can be no assurance as to the level of future dividends. The declaration, payment and amount of any future dividends of the Company are subject to the discretion of the Shareholders or, in the case of interim dividends, to the discretion of the Board and will depend upon, amongst other things, the Company's earnings, financial position, cash requirements, availability of profits, as well as provisions for relevant laws or generally accepted accounting principles from time to time.

Impact of conversion of Loan Notes into Ordinary shares on EIS relief

Immediately prior to the Placing, all of the 2013 Loan Notes will convert into A Shares and all of the 2014 Loan Notes will convert into Ordinary Shares. The A Shares will convert into Ordinary Shares at Admission in accordance with the Existing Articles as further described in paragraph 4.8.7 of Part VI of this document. Holders of Loan Notes who subscribed for shares in the capital of Evgen or, following 5 December 2014, Evgen Pharma and who sought EIS relief after 21 October 2012 and subsequently subscribed for Loan Notes may have some or all of any EIS relief attributable to such shares reduced or withdrawn as a result of such a conversion.

Forward looking statements

This document contains forward-looking statements that involve risks and uncertainties. The Group's results could differ materially from those anticipated in the forward-looking statements as a result of many factors, including the risks faced by the Group, which are described above and elsewhere in the document. Additional risks and uncertainties not currently known to the Directors may also have an adverse effect on the Group's business.

The specific and general risk factors detailed above do not include those risks associated with the Group which are unknown to the Directors.

Although the Directors will seek to minimise the impact of the Risk Factors, investment in the Company should only be made by investors able to sustain a total loss of their investment. Investors are strongly recommended to consult an investment adviser authorised under FSMA who specialises in investments of this nature before making any decision to invest.

PART III

Part III of this document contains: in Section A, the historical financial information of Evgen Pharma plc (and its subsidiary, Evgen Limited) for the three years ended 31 March 2015; in Section B, the accountants' report on the historical financial information in Section A; and in Section C, an unaudited *pro forma* statement of net assets of the Group.

SECTION A: CONSOLIDATED HISTORICAL FINANCIAL INFORMATION ON EVGEN PHARMA PLC FOR THE THREE YEARS ENDED 31 MARCH 2015

Consolidated Statement of Comprehensive income
For the three years ended 31 March 2015

		Year ended 31 March		
		2013	2014	2015
	Note	£'000	£'000	£'000
Operating expenses		(1,078)	(1,040)	(951)
Aborted IPO expenses		—	—	(295)
Total operating expenses	6	(1,078)	(1,040)	(1,246)
Other income	7	131	83	—
Loss from operations		(947)	(957)	(1,246)
Finance costs	9	(1)	(199)	(1,057)
Loss before taxation		(948)	(1,156)	(2,303)
Taxation credit	10	82	79	30
Total comprehensive loss for period attributable to the owners of Evgen Pharma plc		(866)	(1,077)	(2,273)
Loss per share attributable to the owners of Evgen Pharma plc				
		£	£	£
Loss per share – basic	11	(24.65)	(29.54)	(62.34)
Loss per share – diluted	11	(24.65)	(29.54)	(62.34)

All operations were continuing throughout the period.

Consolidated Statement of Financial Position

	Note	As at 31 March 2013 £'000	2014 £'000	2015 £'000
Assets				
Property, plant and equipment	12	2	1	1
Intangible assets	13	58	51	45
Total non-current assets		60	52	46
Trade and other receivables	14	29	97	117
Current tax		108	103	30
Cash and cash equivalents	15	113	314	163
Total current assets		250	514	310
Total assets		310	566	356
Liabilities				
Trade and other payables	16	108	138	477
Current tax		26	50	—
Loans	17	—	2	3
Total current liabilities		134	190	480
Net current assets/(liabilities)		116	324	(170)
Loans	17	—	150	1,063
Other payables	16	—	45	—
Total non-current liabilities		—	195	1,063
Total liabilities		134	385	1,543
Net assets/(liabilities)		176	181	(1,187)
Equity				
Share capital	19	73	73	73
Merger reserve	20	2,067	2,067	2,067
Shares to be issued	21	—	1,000	1,750
Share based compensation	22	229	311	466
Retained deficit		(2,193)	(3,270)	(5,543)
Equity (deficit) attributable to owners of Evgen Pharma plc		176	181	(1,187)

Consolidated Statement of Changes in Equity

For the three years ended 31 March 2015

Attributable to owners of Evgen Pharma plc

	Share Capital £'000	Merger Reserve £'000	Share to be issued £'000	Share based compensation £'000	Retained Earnings £'000	Total Equity £'000
Movements by year						
As at 1 April 2012	62	1,624	—	160	(1,327)	519
Total comprehensive loss for the year	—	—	—	—	(866)	(866)
Transactions with shareholders:						
Share based compensation	—	—	—	69	—	69
Share Issue	11	443	—	—	—	454
As at 31 March 2013	73	2,067	—	229	(2,193)	176
Total comprehensive loss for the year	—	—	—	—	(1,077)	(1,077)
Transactions with shareholders:						
Equity element of loan notes	—	—	1,000	—	—	1,000
Share based compensation	—	—	—	82	—	82
As at 31 March 2014	73	2,067	1,000	311	(3,270)	181
Total comprehensive loss for the year	—	—	—	—	(2,273)	(2,273)
Transactions with shareholders:						
Equity element of loan notes	—	—	750	—	—	750
Share based compensation	—	—	—	155	—	155
As at 31 March 2015	73	2,067	1,750	466	(5,543)	(1,187)

As discussed in more detail under accounting policies, the Group reconstruction has been accounted for in accordance with the principles of merger accounting. For this reason the Group balance sheet has been restated to reflect the effects of the merger, which resulted in 1 Evgen Pharma plc share for every 1 Evgen Limited share in issue at that date.

Consolidated Statement of Cash Flows
For the three years ended 31 March 2015

	Note	Year ended 31 March 2013 £'000	2014 £'000	2015 £'000
Net cash flow from operating activities				
Loss before taxation		(948)	(1,156)	(2,303)
Non-cash Adjustments				
Depreciation and amortisation	6	5	8	7
Finance costs		1	199	1,057
Share based compensation		69	82	155
Working Capital Adjustments				
Decrease/(increase) in trade and other receivables		12	(68)	(20)
Increase in trade and other payables		51	30	101
Tax credit received		33	108	103
Net cash used in operations		(777)	(797)	(900)
Cash flows from investing activities				
Purchase of property, plant and equipment	12	(2)	—	(1)
Acquisition of intangible assets	13	(32)	—	—
Net cash used in investing activities		(34)	—	(1)
Cash flows from financing activities				
Proceeds from issue of convertible loan notes		—	1,000	750
Proceeds from share issue		454	—	—
Interest paid		(1)	(2)	—
Net cash from financing activities		453	998	750
Net (decrease)/increase in cash and equivalents		(358)	201	(151)
Cash and cash equivalents brought forward		471	113	314
Cash and cash equivalents carried forward	15	113	314	163

Notes to the Historical Financial Information

1. Basis of preparation

Evgen Pharma plc (''the Company'') is a public limited company and was incorporated in the United Kingdom on 2 October 2014, and is domiciled in the United Kingdom. The principal activity is the development of pharmaceutical products. There has been no revenue to date.

On 5 December 2014 the Company acquired Evgen Limited (''Evgen''). This transaction did not meet the definition of a business combination as set out in IFRS 3. It is noted that such transactions are outside the scope of IFRS 3 and there is no other guidance elsewhere in IFRS covering such transactions.

IAS 8 Accounting Policies, Changes in Accounting Estimates and Errors, requires that where IFRS does not include guidance for a particular issue, the Directors may also consider the most recent pronouncements of other standard setting bodies that use a similar conceptual framework to develop accounting standards when developing an appropriate accounting policy.

In this regard, it is noted that the UK Accounting Standards Board has, in issue, an accounting standard covering business combinations (FRS 6) that permits the use of the merger accounting principles for such transactions. The Directors have therefore chosen to adopt these principles and the historical financial information has been prepared as if Evgen had been owned and controlled by the Company throughout the year ended 31 March 2013, year ended 31 March 2014 and the year ended 31 March 2015. Accordingly, the assets and liabilities of Evgen have been recognised at their historical carrying amounts, the results for the periods prior to the date the Company legally obtained control have been recognised and the financial information and cash flows reflect those of Evgen. The amount recognised in equity is based on the historical carrying amounts recognised by Evgen. However, the share capital balance is adjusted to reflect the equity structure of the outstanding share capital of the Company, and any corresponding differences are reflected as an adjustment to a merger reserve.

This historical financial information (''Historical Financial Information'') has been prepared by the Directors on a going concern basis under the historical cost convention; in accordance with the requirements of the AIM Rules for Companies, for the purposes of the AIM admission document dated 15 October 2015; and is in accordance with International Financial Reporting Standards (IFRSs) as adopted by the EU, the International Financial Reporting Interpretations Committee (IFRIC) interpretations issued by the International Accounting Standards Boards (''IASB'') that are effective or issued and early adopted as at the time of preparing this Historical Financial Information.

The preparation of Historical Financial Information requires the Directors to exercise their judgement in the process of applying accounting policies. The areas involving a higher degree of judgement or complexity, or areas where assumptions and estimates are significant to the Historical Financial Information are disclosed in note 5.

The Historical Financial Information in this Part III does not constitute statutory accounts within the meaning of Section 434 of the Companies Act 2006.

The Historical Financial Information is presented in sterling and, unless otherwise stated, amounts are expressed in thousands, with rounding accordingly.

The Board of Directors and the Financial Director are together considered the chief operating decision maker.

2. Summary of significant accounting policies

The principal accounting policies adopted are set out below.

2.1. Basis of consolidation

The consolidated financial statements incorporate the financial statements of the Company and entities controlled by the Company (its subsidiaries) made up to 31 March each year. Control is achieved when the Company has the power over the investee; is exposed, or has rights, to variable return from its involvement with the investee; and, has the ability to use its power to affect its returns. The Company reassesses whether or not it controls an investee if facts and circumstances indicate that there are changes to one or more of the three elements of control listed above.

Consolidation of a subsidiary begins when the Company obtains control over the subsidiary and ceases when the Company losses control of the subsidiary. Specifically, the results of subsidiaries acquired or disposed of during the year are included in the consolidated statement of comprehensive income from the date the Company gains control until the date when the Company ceases to control the subsidiary.

Where necessary, adjustments are made to the financial statements of subsidiaries to bring the accounting policies used into line with the Group's accounting policies.

All intragroup assets and liabilities, equity, income, expenses and cash flows relating to transactions between the members of the Group are eliminated on consolidation.

2.2. Going concern

As part of their going concern review the Directors have followed the guidelines published by the Financial Reporting Council entitled ''Guidance on Risk Management and Internal Control and Related Financial and Business Reporting''.

The Directors have prepared detailed financial forecasts and cash flows looking beyond 12 months from the date of this Historical Financial Information. In developing these forecasts the Directors have made assumptions based upon their view of the current and future economic conditions that will prevail over the forecast period.

On the basis of the above projections, the Directors are confident that the Group has sufficient working capital to honour all of its obligations to creditors as and when they fall due. Accordingly, the Directors continue to adopt the going concern basis in preparing the Historical Financial Information.

2.3. Currencies

Functional and presentational currency

Items included in the Historical Financial Information are measured using the currency of the primary economic environment in which the Group operates (''the functional currency'') which is UK sterling (£). The Historical Financial Information is presented in UK sterling.

Transactions and balances

Foreign currency transactions are translated into the functional currency using the exchange rates prevailing at the dates of the transactions or at an average rate for a period if the rates do not fluctuate significantly. Foreign exchange gains and losses resulting from the settlement of such transactions and from the translation at year-end exchange rates of monetary assets and liabilities denominated in foreign currencies are recognised in the statement of comprehensive income. Non-monetary items that are measured in terms of historical cost in a foreign currency are not retranslated.

2.4. Intangible assets

Intangible assets with finite useful lives that are acquired externally are carried at cost less accumulated amortisation and impairment losses. Amortisation is recognised on a straight-line basis over their estimated useful lives as below. The estimated useful life and amortisation method are reviewed at the end of each reporting period, with the effect of any changes in estimate being accounted for on a prospective basis.

Licences – 10 years

2.5. Property, plant and equipment

Property, plant and equipment are stated at cost less accumulated depreciation and any impairment losses. Cost includes the original purchase price of the asset and the costs attributable to bringing the asset to its working condition for its intended use. Such assets acquired in a business combination are initially recognised at their fair value at acquisition date. Depreciation is charged so as to write off the costs of assets over their estimated useful lives, on a straight-line basis starting from the month they are first used, as follows:

Plant, fixtures and fittings – 4 years
IT Equipment – 4 years

The gain or loss arising on the disposal of an asset is determined as the difference between the sales proceeds and the carrying amount of the asset and is recognised in the Statement of Comprehensive Income.

At each reporting date, the Group reviews the carrying amounts of its property, plant and equipment assets to determine whether there is any indication that those assets have suffered an impairment loss. If any such indication exists, the recoverable amount of the asset is estimated in order to determine the extent of the impairment loss (if any).

2.6. Research and development expenditure

All research and development costs, whether funded by third parties under licence and development agreements or not, are included within operating expenses and classified as such. Research and development costs relating to clinical trials are recognised over the period of the clinical trial based on information provided by clinical research organisations. All other expenditure on research and development is recognised as the work is completed.

All ongoing development expenditure is currently expensed in the year in which it is incurred. Due to the regulatory and other uncertainties inherent in the development of the Group's programmes, the criteria for development costs to be recognised as an asset, as prescribed by IAS 38, 'Intangible assets', are not met until the product has been submitted for regulatory approval, such approval has been received and it is probable that future economic benefits will flow to the Group. The Group does not currently have any such internal development costs that qualify for capitalisation as intangible assets.

2.7. Income tax

The tax expense or credit represents the sum of the tax currently payable or recoverable and the movement in deferred tax assets and liabilities.

(a) Current income tax

Current tax is based on taxable income for the year and any adjustment to tax from previous years. Taxable income differs from net income in the statement of comprehensive income because it excludes items of income or expense that are taxable or deductible in other years or that are never taxable or deductible. The calculation uses the latest tax rates for the year that have been enacted or substantively enacted by the dates of the Statement of Financial Position.

(b) Deferred tax

Deferred tax is calculated at the latest tax rates that have been substantially enacted by the reporting date that are expected to apply when settled. It is charged or credited in the Statement of Comprehensive Income, except when it relates to items credited or charged directly to equity, in which case it is also dealt with in equity.

Deferred tax is the tax expected to be payable or recoverable on differences between the carrying amounts of assets and liabilities in the Historical Financial Information and the corresponding tax bases used in the computation of taxable income, and is accounted for using the liability method. It is not discounted.

Deferred tax liabilities are generally recognised for all taxable temporary differences and deferred tax assets are recognised to the extent that it is probable that taxable income will be available against which the asset can be utilised. Such assets are reduced to the extent that it is no longer probable that the asset can be utilised.

Deferred tax assets and liabilities are offset when there is a legal right to offset current tax assets and liabilities and when the deferred tax assets and liabilities relate to taxes levied by the same taxation authority on either the same taxable entity or different taxable entities where there is an intention to settle the balances on a net basis.

2.8. Operating leases

Leases in which a significant portion of the risks and rewards of ownership are retained by the lessor are classified as operating leases. Rentals payable under operating leases (net of any incentives received from the lessor) are charged to the Statement of Comprehensive Income on a straight-line basis over the term of the relevant lease.

2.9. Government grants

Government grants are not recognised until there is reasonable assurance that the Group will comply with the conditions attaching to them and that the grant will be received.

Government grants are recognised as Other Income on a systematic basis over the periods in which the Group recognises the associated expenses. Grants that are receivable as compensation for expenses or losses already incurred or for the purpose of giving immediate financial support to the Group with no future related costs are recognised in the period in which they become receivable.

2.10. Payroll expense and related contributions

Wages, salaries, payroll tax, paid annual leave and sick leave, bonuses, and non-monetary benefits are accrued in the year in which the associated services are rendered.

2.11. Pension costs

The Group has not operated a pension scheme or made any contributions towards staff pensions to date, but will be required to start a scheme under the UK's auto-enrolment rules.

2.12. Share-based compensation

The Group issues share based payments to certain employees and directors. Equity-settled share-based payments are measured at fair value at the date of grant and expensed on a straight-line basis over the vesting period, along with a corresponding increase in equity.

At each reporting date, the Group revises its estimate of the number of equity instruments expected to vest as a result of the effect of non-market-based vesting conditions. The impact of any revision is recognised in statement of comprehensive income, with a corresponding adjustment to equity reserves.

The fair value of share options is determined using a Black-Scholes model, taking into consideration the best estimate of the expected life of the option and the estimated number of shares that will eventually vest.

2.13. Operating segments

Operating segments are reported in a manner consistent with the internal reporting provided to the chief operating decision-maker. The chief operating decision-maker is responsible for allocating resources and assessing performance of operating segments.

The Directors consider that there are no identifiable business segments that are subject to risks and returns different to the core business. The information reported to the Directors, for the purposes of resource allocation and assessment of performance is based wholly on the overall activities of the Group. The Group has therefore determined that it has only one reportable segment under IFRS 8.

The results and assets for this segment can be determined by reference to the statement of comprehensive income and statement of financial position.

2.14. Dividends

Dividends are recognised as a liability and deducted from equity at the time they are approved. Otherwise dividends are disclosed if they have been proposed or declared before the relevant financial statements are approved.

2.15. Accounting developments

New standards, amendments and interpretations adopted during the year ended 31 March 2015

The IASB and IFRIC have issued the following standards and interpretations which have been adopted during the year. The adoption of these standards and interpretations has not had a material impact on the Group.

Standard	Key requirements
IFRS 10, Consolidated Financial Statements	The standard's objective is to establish principles for the presentation and preparation of consolidated financial statements when an entity controls one or more other entities. It builds on existing principles by identifying the concept of control as the determining factor in whether an entity should be included within the consolidated financial statements of the parent company. The standard provides additional guidance to assist in the determination of control where this is difficult to assess.
IFRS 11, Joint Arrangements	IFRS 11 is a more realistic reflection of joint arrangements by focusing on the rights and obligations of the arrangement rather than its legal form. There are two types of joint arrangement: joint operations and joint ventures. Proportional consolidation of joint ventures is no longer allowed.
IFRS 12, Disclosures of interests in Other Entities	IFRS 12 includes the disclosure requirements for all forms of interests in other entities, including joint arrangements, associates, special purpose vehicles and other off balance sheet vehicles.
IAS 27 (revised 2011), Separate Financial Statements	IAS 27 (revised 2011) includes the provisions on separate financial statements that are left after the control provisions of IAS 27 have been included in the new IFRS 10.
IAS 28 (revised 2011), Associates and Joint Ventures	IAS 28 (revised 2011) includes the requirements for joint ventures, as well as associates, to be equity accounted following the issue of IFRS 11.
IAS 32, Offsetting Financial Assets and Financial Liabilities	The amendments clarify existing application issues relating to the offsetting requirements.

New standards, amendments and interpretations issued but not effective for the financial year beginning 1 April 2015 and not early adopted

The IASB and IFRIC have issued the following standards and interpretations with effective dates as noted below:

Standard	Key requirements	Effective date (for annual periods beginning on or after)
IFRS 9, Financial Instruments	The standard is the first standard issued as part of a wider project to replace IAS 39. It replaces the parts of IAS 39 that relate to the classification and measurement of financial instruments. IFRS 9 requires financial assets to be classified into two measurement categories: those measured as at fair value and those measured at amortised cost. The classification depends on the entity's business model and the contractual cash flow characteristics of the instrument. The guidance in IAS 39 on impairment of financial assets and hedge accounting continues to apply.	1 January 2018
IFRS 15, Revenue from Contracts with Customers	The standard specifies how and when a company will recognise revenue as well as requiring such entities to provider users of financial statements with more informative, relevant disclosures. The standard provides a single, principles based five-step model to be applied to all contracts with customers.	1 January 2018

There are no other IFRSs or IFRIC interpretations that are not yet effective that would be expected to have a material impact on the Group.

3. Financial instruments

Financial assets and financial liabilities are recognised in the Group's statement of financial position when the Group becomes party to the contractual provisions of the instrument. Financial assets are de-recognised when the contractual rights to the cash flows from the financial asset expire or when the contractual rights to those assets are transferred. Financial liabilities are de-recognised when the obligation specified in the contract is discharged, cancelled or expired.

3.1. Trade and other receivables

Trade and other receivables are recognised initially at fair value and subsequently measured at amortised cost using the effective interest method less provision for impairment. Appropriate provisions for estimated irrecoverable amounts are recognised in the statement of comprehensive income when there is objective evidence that the assets are impaired. Interest income is recognised by applying the effective interest rate, except for short-term receivables when the recognition of interest would be immaterial.

3.2. Cash and cash equivalents

Cash and cash equivalents consist of cash on hand, demand deposits, and other short-term highly liquid investments that are readily convertible to a known amount of cash and are subject to an insignificant risk of changes in value.

3.3. Trade and other payables

Trade and other payables are initially measured at their fair value and are subsequently measured at their amortised cost using the effective interest rate method; this method allocates interest expense over the relevant period by applying the ''effective interest rate'' to the carrying amount of the liability.

3.4. Classification as debt or equity

Debt and equity instruments issued by the Group are classified as either financial liabilities or as equity in accordance with the substance of the contractual arrangements and the definitions of a financial liability and an equity instrument.

3.5. Equity instruments

An equity instrument is any contract that evidences a residual interest in the assets of an entity after deducting all of its liabilities. Equity instruments issued by the Group are recognised at the proceeds received, net of direct issue costs.

3.6. Compound instruments

The component parts of compound instruments (convertible notes) issued by the Group are classified separately as financial liabilities and equity in accordance with the substance of the contractual arrangements and the definitions of a financial liability and equity instrument.

The conversion option classified as equity is determined by deducting the amount of the liability component from the fair value of the compound instrument as a whole. This is recognised and included in equity, net of income tax effects, and is not subsequently remeasured. In addition, the conversion option classified as equity will remain in equity until the conversion option is exercised, in which case, the balance recognised in equity will be transferred to other equity. When the conversion option remains unexercised at maturity date of the convertible note, the balance recognised in equity will be transferred to retained earnings. No gain or loss is recognised upon conversion or expiry of the conversion option.

Transaction costs that relate to the issue of the convertible notes are allocated to the liability and equity components in proportion to the allocation of gross proceeds. Transaction costs relating to the equity component are recognised directly in equity. Transaction costs relating to the liability component are included in the carrying value of the liability component and are amortised over the lives of the convertible notes using the effective interest method.

Liabilities other than those classified as fair value through profit or loss are initially recorded at fair value net of transaction costs. Transaction costs and other finance costs are amortised to the profit and loss over the expected life of the instrument using the effective interest

method. Subsequently, if the expected life of the instrument is revised the carrying value of the instrument is revised to reflect the present value of the future cash flows discounted at the original effective interest rate. Any adjustments to the carrying value are recognised in the Statement of Comprehensive Income.

4. Financial risk management

4.1. Financial risk factors

The Group's activities expose it to certain financial risks: market risk, credit risk and liquidity risk. The overall risk management programme focuses on the unpredictability of financial markets and seeks to minimise potential adverse effects on the Group's financial performance. Risk management is carried out by the Directors, who identify and evaluate financial risks in close co-operation with key staff.

(a) Market risk

Market risk is the risk of loss that may arise from changes in market factors such as competitor pricing, interest rates, foreign exchange rates.

(b) Credit risk

Credit risk is the financial loss to the Group if a customer or counterparty to financial instruments fails to meet its contractual obligation. Credit risk arises from the Group's cash and cash equivalents and receivables balances.

(c) Liquidity risk

Liquidity risk is the risk that the Group will not be able to meet its financial obligations as they fall due. This risk relates to the Group's prudent liquidity risk management and implies maintaining sufficient cash. The Directors monitor rolling forecasts of the Group's liquidity and cash and cash equivalents based on expected cash flow.

4.2. Capital risk management

The Group is funded by equity and loans. The components of shareholders' equity are:

(a) The share capital and share premium account arising on the issue of shares.

(b) Merger reserve, which was created as a result of the acquisition by the Company of the entire issued share capital of Evgen on 5 December 2014 (see note 20). This reserve is not considered to be distributable; and retained deficit, which reflects losses incurred to date.

(c) The shares to be issued reserve arising in relation to the convertible loan note

(d) The share based compensation reserve results from the Group's grant of equity-settled share options to selected employees and Directors;

(e) The retained reserve or deficit reflecting comprehensive income to date.

The Group's objective when managing capital is to maintain adequate financial flexibility to preserve its ability to meet financial obligations, both current and long term. The capital structure of the Group is managed and adjusted to reflect changes in economic conditions. The Group funds its expenditures on commitments from existing cash and cash equivalent balances, primarily received from issuances of shareholders equity. There are no externally imposed capital requirements. Financing decisions are made based on forecasts of the expected timing and level of capital and operating expenditure required to meet the Group's commitments and development plans.

4.3. Fair value estimation

The carrying value less impairment provision of trade receivables and payables are assumed to approximate their fair values because of the short-term nature of such assets and the effect of discounting liabilities is negligible.

5. Critical accounting estimates and judgements

The preparation of this Historical Financial Information requires management to make judgements and estimates that affect the reported amounts of assets and liabilities at each Statement of Financial Position date and the reported amounts of revenue during the reporting periods. Actual results could differ from these estimates. Information about such judgements and estimations are

contained in individual accounting policies. The key judgements and sources of estimation uncertainty that could cause an adjustment to be required to the carrying amount of asset or liabilities within the next accounting period are outlined below:

5.1. Share based payment charge

During the years ended 31 March 2013, 31 March 2014 and 31 March 2015, the Group issued a number of share options to certain employees. The Black-Scholes model was used to calculate the appropriate charge for that and subsequent years.

The use of this model to calculate a charge involves using a number of estimates and judgements to establish the appropriate inputs to be entered into the model, covering areas such as the use of an appropriate interest rate and dividend rate, exercise restrictions and behavioural considerations. A significant element of judgement is therefore involved in the calculation of the charge.

The total charge recognised in the year to 31 March 2013 £69,000, year to 31 March 2014 £82,000, and year to 31 March 2015 £155,000. Further information on share options can be found in note 22.

5.2. Convertible loans

During the year ended 31 March 2014, the Group issued convertible loan notes of £1,000,000. Transaction costs relating to the liability component of £1,000,000 are amortised over the lives of the convertible notes using the effective interest method.

During the year ended 31 March 2015, the Group issued convertible loan notes of £750,000. Transaction costs relating to the liability component of £750,000 are amortised over the lives of the convertible notes using the effective interest method.

Subsequently, if the expected life of the instrument is revised the carrying value of the instrument is revised to reflect the present value of the future cash flows discounted at the original effective interest rate. Any adjustments to the carrying value are recognised in profit and loss. Further information can be found in note 17.

6. Operating Expenses

The loss is stated after charging expenses as follows:

	Year to 31 March		
	2013	**2014**	**2015**
	£'000	**£'000**	**£'000**
Research and development:			
Royalty payments	32	—	—
Amortisation of licences	4	7	6
Other research and development	573	498	196
Staff costs – Note 8	338	373	437
Establishment and general:			
Foreign exchange loss/gain	(14)	—	—
Operating lease costs – land and buildings	5	5	5
Depreciation of owned property, plant and equipment	1	1	1
Aborted IPO expenses	—	—	295
Other operating expenses	139	156	306
Total operating expenses	1,078	1,040	1,246

The Group has one reportable segment, namely the development of pharmaceutical products all within the United Kingdom.

7. Other income

	Year to 31 March		
	2013 £'000	2014 £'000	2015 £'000
Government grants receivable	131	83	—

8. Staff and Remuneration

8.1. Number of staff

	Year to 31 March		
	2013 No	2014 No	2015 No
Average number of employees (including directors):			
Management	1	1	1
Development	1	1	1
Administrative	—	1	1
Non-executive	2	4	4
	4	7	7

8.2. Remuneration

	Year to 31 March		
	2013 £'000	2014 £'000	2015 £'000
Aggregate remuneration of staff (including directors):			
Wages and salaries	214	233	237
Social security costs	55	58	45
Share-based payments	69	82	155
	338	373	437

8.3. Directors' Remuneration

Remuneration of the Directors who are the key members of management, within statement of comprehensive income:

	Year to 31 March		
	2013 £'000	2014 £'000	2015 £'000
Short-term remuneration	214	216	220
Social security costs	55	58	45
	269	274	265
Remuneration of highest paid director	95	95	95

9 Finance costs

	Year to 31 March		
	2013 £'000	2014 £'000	2015 £'000
Interest payable on fair value of loan notes	—	198	1,057
Other interest and similar charges	1	1	—
	1	199	1,057

10 Taxation

10.1. Net tax credit

	Year to 31 March		
	2013	**2014**	**2015**
	£'000	**£'000**	**£'000**
Current tax			
Current period – UK corporation tax (Note 10.2)	—	—	—
Adjustment for prior periods – R&D tax credits	82	79	30
Net tax credit	82	79	30

10.2. Factors affecting the tax charge

Tax is assessed for the period at a rate different to the UK corporate tax rate for the reasons below:

	Year to 31 March		
	2013	**2014**	**2015**
UK corporate tax rate	24%	23%	21%
	£'000	**£'000**	**£'000**
Net income before taxation	(948)	(1,156)	(2,303)
Tax at the UK corporate tax rate	(228)	(266)	(484)
Other adjustment	228	266	484
Research and development tax credits	82	79	30
Tax for the period	82	79	30

10.3. Factors that may affect future tax charges

The rate of UK Corporation tax for the period to 31 March 2014 was 23 per cent., and 21 per cent. with effect from 1 April 2014. During the year a further reduction to 20 per cent. with effect from 1 April 2015 was enacted.

As at 31 March 2015, the Group had unrecognised deferred tax assets totalling £570,000 (2014: £460,000, 2013: £340,000) which primarily relates to losses. The Group has not recognised this as an asset in the consolidated statement of financial position due to the uncertainty in the timing of its crystallisation.

11. Earnings per share

Basic earnings per share is calculated by dividing the net income for the period attributable to ordinary equity holders by the weighted average number of ordinary shares outstanding during the period.

In the case of diluted amounts, the denominator also includes ordinary shares that would be issued if any dilutive potential ordinary shares were converted.

The basic and diluted calculations are both based on the following:

	Year to 31 March		
	2013	2014	2015
	£'000	£'000	£'000
Loss for the period	(866)	(1,077)	(2,273)
	Number	**Number**	**Number**
Weighted average number of shares – basic	35,126	36,462	36,462
Share options	—	—	—
Weighted average number of shares – diluted	35,126	36,462	36,462
	£	**£**	**£**
Loss per share – basic	(24.65)	(29.54)	(62.34)
Loss per share – diluted	(24.65)	(29.54)	(62.34)

The loss and the weighted average number of ordinary shares for the three years ended 31 March 2015 used for calculating the diluted loss per share are identical to those for the basic loss per share. This is because the outstanding share options would have the effect of reducing the loss per ordinary share and would therefore not be dilutive under the terms of International Accounting Standard (''IAS'') No 33.

12. Property, plant and equipment

Movements by year

	Plant, fixtures and fittings £'000	IT equipment £'000	Total £'000
Cost:			
As at 1 April 2012	1	1	2
Additions	—	2	2
As at 31 March 2013	1	3	4
As at 31 March 2014	1	3	4
Additions	—	1	1
As at 31 March 2015	1	4	5
Accumulated depreciation:			
As at 1 April 2012	—	1	1
Charge for the period	—	1	1
As at 31 March 2013	—	2	2
Charge for the period	—	1	1
As at 31 March 2014	—	3	3
Charge for the period	1	—	1
As at 31 March 2015	1	3	4
Carrying amount:			
As at 1 April 2012	1	—	1
As at 31 March 2013	1	1	2
As at 31 March 2014	1	—	1
As at 31 March 2015	—	1	1

These and all other group assets have been pledged in security for the loan (Note 17).

The depreciation charge for the year has been included in Operating Expenses in the Statement of Comprehensive Income.

13. Intangible Assets

Movements by year

	Licences £'000
Cost:	
As at 1 April 2012	32
Additions	32
As at 31 March 2013	64
Additions	—
As at 31 March 2014	64
Additions	—
As at 31 March 2015	64
Accumulated amortisation:	
As at 1 April 2012	2
Charge for the period	4
As at 31 March 2013	6
Charge for the period	7
As at 31 March 2014	13
Charge for the period	6
As at 31 March 2015	19
Carrying Amount	
As at 1 April 2012	30
As at 31 March 2013	58
As at 31 March 2014	51
As at 31 March 2015	45

The recoverable amounts were measured based on value in use.

The amortisation charge for the year has been included in Operating Expenses in the Statement of Comprehensive Income.

14. Trade and other receivables

	As at 31 March		
	2013 £'000	2014 £'000	2015 £'000
Trade receivables	—	8	6
VAT recoverable	11	30	54
Other receivables	—	—	16
Prepayments	18	59	41
	29	97	117

The Directors believe that the carrying value of trade and other receivables represents their fair value. In determining the recoverability of trade receivables, the Group considers any change in the credit quality of the receivable from the date credit was granted up to the reporting date.

Details on the Group's credit risk management policies are shown in Note 18. The Group does not hold any collateral as security for its trade and other receivables.

15. Cash and cash equivalents

	As at 31 March		
	2013	2014	2015
	£'000	£'000	£'000
Cash and cash equivalents	113	314	163

The Group's cash and cash equivalents do not currently earn interest. The Directors consider that the carrying value of cash and cash equivalents approximates to their fair value.

16. Trade and other payables

	As at 31 March		
	2013	2014	2015
	£'000	£'000	£'000
Trade payables	28	18	130
Accruals	10	6	201
Employee tax and social security	70	114	146
	108	138	477
Non current:			
Other payables	—	45	—

17. Borrowings

	As at 31 March		
	2013	2014	2015
	£'000	£'000	£'000
Current			
Convertible loan notes	—	2	3
Non-current			
Convertible loan notes	—	150	1,063
Total borrowings	—	152	1,066

The earliest that the lenders of the above non-current borrowings require repayment is as follows:

Between one and two years			
Convertible loan notes	—	2	3
Between two and five years			
Convertible loan notes	—	150	1,063
	—	152	1,066
Element of the loans treated as equity:	—	1,000	1,750

Trade and other payables principally consist of amounts outstanding for trade purchases and ongoing costs. They are non-interest bearing and are normally settled on 30 to 45 day terms.

The Directors consider that the carrying value of trade and other payables approximates their fair value. All trade and other payables are denominated in Sterling. Evgen has financial risk management policies in place to ensure that all payables are paid within the credit timeframe and no interest has been charged by any suppliers as a result of late payment of invoices during the period.

On 2 July 2013 and on 30 October 2013, unsecured convertible loan notes with an aggregate nominal value of £85,000 and £915,000 respectively were issued (together "2013 Notes").

The 2013 Notes are repayable bi-annually on the basis of 1/1000 of the principal outstanding (plus accrued but unpaid interest) being paid each year until 30 April 2017 when all remaining

outstanding 2013 Notes will be repaid with all unpaid interest. Interest accrues daily on the 2013 Notes at a rate of 11 per cent. per annum, which is rolled up and either paid on the relevant repayment date, or converted into shares in Evgen on the occurrence of a conversion event.

The 2013 Notes holders may convert to A Ordinary Shares at £42.46 per share at any time. On a qualified fund raising or qualified listing, the outstanding 2013 Notes together with all accrued and unpaid interest, will convert automatically into fully paid A Ordinary Shares at a price per share being a 50 per cent. discount to the Placing Price immediately prior to Admission.

On 3 November 2014, unsecured convertible loan notes with an aggregate nominal value of £750,000 were issued (together "2014 Notes").

The 2014 Notes are repayable bi-annually on the basis of 1/1000 of the principal outstanding (plus accrued but unpaid interest) being paid each year until 2 January 2017 when all remaining outstanding outstanding 2014 Notes will be repaid with all unpaid interest. Interest accrues daily on the 2014 Notes at a rate of 11 per cent. per annum, which is rolled up and either paid on the relevant repayment date, or converted into shares in Evgen on the occurrence of a conversion event.

Transaction costs relating to the liability component are included in the carrying value of the liability component and are amortised over the lives of the convertible notes using the effective interest method. Subsequently, if the expected life of the instrument is revised the carrying value of the instrument is revised to reflect the present value of the future cash flows discounted at the original effective interest rate. Any adjustments to the carrying value are recognised in profit and loss.

On a qualified fund raising or qualified listing, the outstanding 2014 Notes together with all accrued and unpaid interest, will convert automatically into fully paid Ordinary Shares at a price per share being a 20 per cent. discount to the Placing Price immediately prior to Admission.

All loans are denominated in sterling.

18. Financial Instruments

The Group is exposed to the risks that arise from its financial instruments. The policies for managing those risks and the methods to measure them are described in Note 4. Further quantitative information in respect of these risks is presented below and throughout this Historical Financial Information.

18.1. Capital Risk management

The Group is funded by equity and loans. Loans were outstanding as shown in Note 17.

18.2. Principal financial instruments

The principal financial instruments used by the Group, from which financial instrument risk arises are as follows:

	As at 31 March		
	2013	**2014**	**2015**
	£'000	**£'000**	**£'000**
Trade and other receivables	11	38	76
Trade and other payables	98	132	276
Cash and cash equivalents	113	314	163

18.3. Financial assets by category

The Group held the following financial assets:

Loans and receivables

	As at 31 March		
	2013	**2014**	**2015**
	£'000	**£'000**	**£'000**
Cash and cash equivalents	113	314	163
Trade receivables	—	8	6
Other receivables	11	30	70
	124	352	239

18.4. Financial liabilities by category

The Group held the following financial liabilities, all of which were classified as other financial liabilities:

Other financial liabilities
At amortised cost

	As at 31 March		
	2013	**2014**	**2015**
	£'000	**£'000**	**£'000**
Trade payables	28	18	130
Borrowings	—	152	1,066
Other payables	70	114	146
	98	284	1,342

18.5. Market Risk

The Group's activities expose it primarily to the financial risks of changes in foreign currency exchange rates and interest rates. In the period of the Historical Financial Information, both these risks are considered to have been minimal.

18.6. Credit Risk

The Group gives careful consideration to which organisations it uses for banking in order to minimise credit risk. The Group holds cash with one large bank in the UK, an institution with a AA credit rating (long term, as assessed by Moody's). The amounts of cash held with that bank at the reporting date can be seen in the financial assets table above. All of the cash and equivalents held with that bank were denominated in UK sterling.

There was no significant concentration of credit risk at the reporting date.

The carrying amount of financial assets recorded in the Historical Financial Information, net of any allowances for losses, represents the Group's maximum exposure to credit risk without taking account of the value of any collateral obtained.

No allowance has been made for impairment losses. In the Directors' opinion, there has been no other impairment of financial assets during the period. An allowance for impairment is made where there is an identified loss event which, based on previous experience, is evidence of a reduction in the recoverability of the cash flows. The Directors consider the above measures to be sufficient to control the credit risk exposure. No collateral is held by the Group as security in relation to its financial assets.

18.7. Liquidity Risk Management

The Directors manage liquidity risk by regularly reviewing the Group's cash requirements by reference to short term cashflow forecasts and medium term working capital projections.

18.8. Foreign Currency Risk Management

The Group's exposure to foreign currency risk has been limited; most of its invoicing and the payments are in sterling. Accordingly, no sensitivity analysis is presented in this area as it is immaterial.

18.9. Maturity of financial assets and liabilities

All of the Group's non-derivative financial liabilities and its financial assets at the reporting date are either payable or receivable within one year, except for borrowings as disclosed in Note 17.

19. Share Capital

Number of shares in issue

	As at 31 March 2015	
	Number	**£000**
Issued and fully paid:		
Issued subscriber Ordinary share of £2	1	—
Issued to former shareholders of Evgen:		
Ordinary shares of £2	12,595	25
Ordinary A shares of £2	18,849	38
Ordinary B shares of £2	5,017	10
Total shares	36,462	73

On 2 October 2014 the Company was incorporated with one ordinary share of £2.00 was subscribed for £nil paid.

On 5 December 2014 the Company entered into an agreement to acquire the entire share capital of Evgen, satisfied by the issue of 12,595 ordinary shares of £2.00 each, 18,849 ordinary A shares of £2.00 each and 5,017 ordinary B shares of £2.00 and the original ordinary share credited as being fully paid.

The three classes of Ordinary shares above have full rights in respect of voting and rank *pari passu* in respect of dividends, capital distributions and winding up.

As detailed in the basis of preparation under note 1 the amount recognised in equity is based on the historical carrying amounts recognised by Evgen. However, the share capital balance is adjusted to reflect the equity structure of the outstanding stock of the Company, and any corresponding differences are reflected as an adjustment to merger reserve.

20. Merger Reserve

The acquisition of its principal and only subsidiary at the period end by the Group does not meet the definition of a business combination and therefore falls outside the scope of IFRS3. The acquisition has therefore been accounted for in accordance with the principles of merger accounting as set out in Financial Reporting Standard 6 – Acquisitions and Mergers.

The consideration paid to the shareholders of Evgen was satisfied by the issue of 12,596 ordinary shares of £2.00 each, 18,849 ordinary A shares of £2.00 each and 5,017 ordinary B shares of £2.00. A merger reserve arises on consolidation being the difference between the nominal value of the shares issued on acquisition and the share capital and share premium of Evgen.

21. Shares to be issued

	As at 31 March		
	2013	**2014**	**2015**
	£000	**£000**	**£000**
Equity element of convertible loan (Note 17)	—	1,000	1,750

22. Share options

Details of the number of share options and the weighted average exercise price (‘‘WAEP’’) outstanding during each period are as follows:

	31 March 2013		31 March 2014		31 March 2015	
	Number	WAEP £	Number	WAEP £	Number	WAEP £
Outstanding at the begininng of the year	5,617	25	5,957	26	8,739	26
Granted during the year	340	40	2,782	29	1,271	7
Cancelled during the year	—	—	—	—	(1,271)	(7)
Outstanding at the end of the year	5,957	26	8,739	26	8,739	26

Over several years options over Ordinary shares have been granted to certain directors and employees under the schemes (the ‘‘Share Schemes’’). Vesting periods have been no more than 2 years, and there have been various exercise prices, some with additional performance conditions attached. They all expire 10 years from the grant date.

Grant date	Number	Option price	Date from which exercisable	Expiry date
24 July 2008	100	£58.37	1 September 2008	24 July 2018
18 August 2010	1,162	£7.00	Performance related	18 August 2020
11 January 2011	180	£7.00	Performance related	11 January 2021
25 November 2011	2,904	£40.00	Performance related	25 November 2021
1 May 2012	340	£40.00	Performance related	1 May 2022
14 August 2013	356	£84.92	Performance related	14 August 2023
23 December 2013	2,426	£21.23	Performance related	23 December 2023
21 November 2014	166	£7.00	Performance related	21 November 2024
21 November 2014	1,105	£7.11	Performance related	21 November 2024
	8,739			

The Group has accounted for the charge arising from the issue of share options as below.

The total charge recognised in the year to 31 March 2013 is £69,000, in the year to 31 March 2014 is £82,000 and in the year to 31 March 2015 is £155,000.

The fair values of the options granted have been calculated using a Black-Scholes model.

Assumptions used were an option life of 5 years, a risk free rate of 2 per cent., a volatility of 60 per cent. and no dividend yield. Other inputs were as follows:

	As at 31 March		
	2013	2014	2015
Number granted	340	2,782	1,271
Assumed share price at grant date (£)	£48.99	£63.69	£148.22
Exercise price (£)	£40.00	£84.92 & £21.23	£7.00 & £7.11
Fair value of each option (£)	£20.16	£13.77 & £46.46	£141.89 & £141.99

23. Ultimate controlling party

In the opinion of the Directors there is no single controlling party.

24. Related party transactions

24.1 Remuneration of key personnel

	As at 31 March		
	2013 £'000	2014 £'000	2015 £'000
Short term remuneration	214	216	220
Social security costs	55	58	45
Share-based payments	62	73	153
	331	347	418

24.2 Transactions and related companies and businesses

	As at 31 March		
	2013 £'000	2014 £'000	2015 £'000
Accounting Services:			
Bradshaw Daniel Limited	—	—	13
Monitoring fees paid to shareholders:			
SPARK Impact, manager of North West Fund for Biomedical	14	15	21
Enterprise Ventures, manager of RisingStars Growth Fund II	14	15	21
Amounts owed by related parties carried forward	28	30	55

	As at 31 March		
	2013 £'000	2014 £'000	2015 £'000
Loan notes issued to related parties:			
RisingStars Growth Fund II	—	230	100
North West Fund for Biomedical	—	545	550
Clarat Partners LLP	—	15	15
	—	790	650

	As at 31 March		
	2013 £'000	2014 £'000	2015 £'000
Interest on Loan notes issued to related parties:			
RisingStars Growth Fund II	—	11	30
North West Fund for Biomedical	—	27	84
Clarat Partners LLP	—	1	2
	—	39	116

25. Principal Subsidiaries

The Company owns 100 per cent. of the issued share capital of Evgen which is incorporated in England and Wales.

26. Operating lease arrangements

Outstanding commitments for future minimum lease payments under non-cancellable operating leases were as follows:

	As at 31 March		
	2013 £'000	2014 £'000	2015 £'000
Within one year	3	3	3
In the second to fifth years inclusive	—	3	—
	3	6	3

Since March 2014, the Group's main facility has been leased at an annual rental of £3,288, payable monthly, together with insurance and service charges. The lease expires in February 2016.

27. Subsequent events

On 25 June 2015, the Company and holders of Evgen Options entered into documentation whereby the holders of Evgen Options over Ordinary Shares in Evgen surrendered their Evgen Options in exchange for the Company granting them replacement Company Options over Ordinary Shares. All replacement Company Options were granted on the same terms as the existing Evgen Options.

On 25 June 2015, a deed of novation was entered into between the Company and Evgen pursuant to which the Company agreed to assume the outstanding rights, interests, liabilities, obligations of Evgen under the 2013 Notes and the 2014 Notes.

On 26 August 2015, 9,569 ordinary shares of £2.00 each in the share capital of the Company were allotted at £209 each.

On 12 October 2015:

a) each ordinary share of £2 each in the share capital of the Company was subdivided into 800 Ordinary Shares of £0.0025 each;

b) each A ordinary share of £2 each in the share capital of the Company was subdivided into 800 A Shares of £0.0025 each; and

c) each B ordinary share of £2 each in the share capital of the Company was subdivided into 800 B Shares of £0.0025 each,

such shares having the same rights and being subject to the same restrictions as set out in the Existing Articles (the "Sub-division"), resulting in there being 17,732,000 Ordinary Shares of £0.0025 each, 15,079,200 A Shares of £0.0025 each and 4,013,600 B Shares of £0.0025 each in issue.

On 14 October 2015, the Company re-registered as a public limited company and changed its name to Evgen Pharma plc.

There have been no other substantial events since the period that require disclosure.

SECTION B: ACCOUNTANTS' REPORT ON EVGEN PHARMA PLC

The following is the full text of a report on Evgen Pharma plc from Baker Tilly Corporate Finance LLP, the Reporting Accountants, to the Directors of Evgen Pharma plc.

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The Directors
Evgen Pharma plc
Liverpool Science Park Innovation Centre 2
146 Brownlow Hill
Liverpool
Merseyside
L3 5RF

15 October 2015

Dear Sirs,

Evgen Pharma plc (''the Company'') and its subsidiary, Evgen Limited (together ''the Group'')

We report on the financial information of the Group (the ''Historical Financial Information'') set out in Section A of Part III of the Admission Document dated 15 October 2015 (''Admission Document'') of the Company. This Historical Financial Information has been prepared for inclusion in the Admission Document on the basis of the accounting policies set out at Note 2 to the Historical Financial Information. This report is required by paragraph 20.1 of Annex I of Appendix 3.1.1 of the Prospectus Rules as applied by part (a) of Schedule Two to the AIM Rules and is given for the purpose of complying with that paragraph and for no other purpose.

Save for any responsibility arising under paragraph 20.1 of Annex I of Appendix 3.1.1 of the Prospectus Rules as applied by part (a) of Schedule Two to the AIM Rules to any person as and to the extent there provided, to the fullest extent permitted by law, we do not accept or assume responsibility and will not accept any liability to any other person for any loss suffered by any such other person as a result of, arising out of, or in connection with this report or our statement, required by and given solely for the purposes of complying with paragraph 20.1 of Annex I of Appendix 3.1.1 of the Prospectus Rules as applied by part (a) of Schedule Two to the AIM Rules for companies, or consenting to its inclusion in the Admission Document.

Responsibilities

The Directors of the Company are responsible for preparing the Historical Financial Information, as set out in Section A of this Part III, in accordance with International Financial Reporting Standards as adopted by the European Union.

It is our responsibility to form an opinion on the Historical Financial Information and to report our opinion to you.

Basis of opinion

We conducted our work in accordance with Standards for Investment Reporting issued by the Financial Reporting Council in the United Kingdom. Our work included an assessment of evidence relevant to the amounts and disclosures in the Historical Financial Information. It also included an assessment of significant estimates and judgments made by those responsible for the preparation

of the Historical Financial Information and whether the accounting policies are appropriate to the entity's circumstances, consistently applied and adequately disclosed.

We planned and performed our work so as to obtain all the information and explanations we considered necessary in order to provide us with sufficient evidence to give reasonable assurance that the Historical Financial Information is free from material misstatement whether caused by fraud or other irregularity or error.

Opinion

In our opinion, the Historical Financial Information gives, for the purposes of the Admission Document, a true and fair view of the state of affairs of the Group as at the dates stated and of its results, cash flows and changes in equity for the periods then ended in accordance with International Financial Reporting Standards as adopted by the European Union.

Declaration

For the purposes of part (a) of Schedule Two to the AIM Rules for companies we are responsible for this report as part of the Admission Document and declare that we have taken all reasonable care to ensure that the information contained in this report is, to the best of our knowledge, in accordance with the facts and contains no omission likely to affect its import. This declaration is included in the Admission Document in compliance with item 1.2 of Annex I and item 1.2 of Annex III of Appendix 3.1.1 of the Prospectus Rules as applied by part (a) of Schedule Two to the AIM Rules.

Yours faithfully

Baker Tilly Corporate Finance LLP

Regulated by the Institute of Chartered Accountants in England and Wales

Baker Tilly Corporate Finance LLP is a limited liability partnership registered in England and Wales, registered no. OC325347. A list of the names of members is open to inspection at the registered office 25 Farringdon Street, London, EC4A 4AB.

SECTION C: UNAUDITED PRO FORMA STATEMENT OF AGGREGATED NET ASSETS

Set out below is an unaudited *pro forma* statement of net assets of Evgen Pharma plc (''the Group'') (the ''*pro forma* financial information'') which has been prepared on the basis of the historical financial information as set out in Section A of this Part III. The *pro forma* financial information has been prepared in a manner consistent with the accounting policies adopted by the Group in preparing such information and on the basis set out in the notes below.

The *pro forma* financial information has been prepared to illustrate the net assets of the Group as if the following events have occurred on 31 March 2015: (i) Pre-IPO Round, (ii) the Conversion (as referred to in paragraph 4.8.5 of Part VI of this document) and (iii) the net proceeds of the Placing had been received.

It is the sole responsibility of the Directors to prepare the *pro forma* financial information. It has been prepared for illustrative purposes only and, because of its nature, addresses a hypothetical situation and, therefore, does not represent the Group's actual financial position or results. Future results of operations may differ materially from those presented in the *pro forma* financial information due to various factors.

			Adjustments			
	Note	The Group (consolidated) as at 31 March 2015 £'000 (1, 2)	Pre-IPO Round £'000 (3)	Conversion £'000 (4)	Placing proceeds £'000 (5)	*Pro forma* net assets (unaudited) as at 31 March 2015 £'000
Assets						
Non current assets						
Property, plant and equipment		1		—	—	**1**
Intangible assets		45			—	**45**
		46	**—**	**—**	**—**	**46**
Current assets						
Trade & other receivables		117	—	—	—	**117**
Current tax		30	—	—	—	30
Cash and cash equivalents		163	1,714	—	6,300	**8,177**
		310	**1,714**	**—**	**6,300**	**8,324**
Total assets		**356**	**1,714**	**—**	**6,300**	**8,370**
Liabilities						
Current liabilities						
Trade and other payables		(477)	—	—	—	**(477)**
Loans		(3)	—	3	—	**—**
		(480)	**—**	**3**	**—**	**(477)**
Non-current liabilities						
Loans		(1,063)	—	1,063	—	**—**
		(1,063)	**—**	**1,063**	**—**	**—**
Total liabilities		**(1,543)**	**—**	**1,066**	**—**	**(477)**
Net (liabilities)/assets		**(1,187)**	**1,714**	**1,066**	**6,300**	**7,893**

1 The net assets figures of Evgen Pharma plc have been extracted without material adjustment from the consolidated historical financial information of the Group contained in Section A of Part III of this document.

2 The *pro forma* statement of net assets has been prepared in a manner consistent with the accounting policies adopted by the Group for the year ended 31 March 2015.

3 The gross proceeds of the Pre-IPO Round were £2.0 million from the issue of 9,569 Ordinary shares at £209 per share. The proceeds of the Pre-IPO Round are stated after deducting related costs of £125,000 and additional aborted IPO costs of £161,000 which were deferred.

4 Immediately prior to the Placing, all of the 2013 Loan Notes will convert into A Shares and all of the 2014 Loan Notes will convert into Ordinary Shares. The A Shares will convert into Ordinary Shares at Admission in accordance with the Existing Articles as further described in paragraph 4.8.7 of Part VI of this document.

5 The gross proceeds of the Placing are expected to be £7.0 million from the issue of 18,918,919 Ordinary shares at £0.37 per share. The proceeds of the Placing are stated after deducting costs relating to the Placing and Admission of approximately £700,000.

6 No account has been taken of any movement in net assets of the Group since 31 March 2015, nor of any other event save as disclosed above.

PART IV

PATENT ATTORNEY'S REPORT

The Directors
Evgen Pharma plc
Liverpool Science Park
Innovation Centre 2
146 Brownlow Hill
Liverpool
L3 5RF

The Directors
Northland Capital Partners Limited
131 Finsbury Pavement
London
EC2A 1NT

15 October 2015

Dear Sirs,

Re: Evgen Pharma plc's Intellectual Property Position
Patent Attorney's Report

HGF Limited ("HGF") is instructed by the directors of Evgen Pharma plc (the "Company") and Northland Capital Partners Limited to prepare a report on the patent and trade mark portfolio currently in the name of Evgen Limited ("Evgen") and its Intellectual Property strategy for inclusion in the Company's admission document dated 15 October 2015. This report comprises the following sections:

This report comprises the following sections:

1. The relationship between HGF and the Company;
2. An outline of the Intellectual Property registration systems which are relevant to the Company;
3. An outline of the Intellectual Property strategy of Evgen;
4. An overview of the proprietary technology of the Company;
5. The Status of the patent and trade mark rights upon which the Company relies; and
6. Third party rights of relevance to the Company.

1. THE RELATIONSHIP BETWEEN HGF AND EVGEN

In January 2012 Harrison Goddard & Foote LLP (which has now been incorporated as HGF Limited) took over management of the patents and patent applications for which Evgen have assumed control (discussed in Section 5 below). Dr Andrew Wells (the managing partner of the Manchester office of HGF and a shareholder in HGF Limited) and Dr Paul Banford (a consultant to HGF) manage the prosecution and maintenance of these patent and patent applications.

Bioscience IP Limited has been working with Evgen since December 2011 and has provided IP strategic advice and conducted a patent landscaping exercise on behalf of the Company. Bioscience IP Limited was founded by Dr Paul Banford in 2010 and he introduced Evgen to the services of HGF.

Ms Sally Cooper is responsible for managing Evgen's trade mark portfolio. She is a qualified trade mark attorney who is not connected to HGF or Bioscience IP Limited. HGF have independently reviewed Evgen's trade mark portfolio for the purposes of this report.

Andrew Wells has a Bachelor of Pharmacy degree (BPharm) and PhD in pharmaceutical sciences; is a Chartered Patent Attorney and a European Patent Attorney; and has been assisting clients to protect inventions in the pharmaceutical field since 2000.

Paul Banford has a BSc and PhD in the biological sciences; is a Chartered Patent Attorney and a European Patent Attorney; and has been assisting clients to protect inventions in the life science field since 1995.

Each of Andrew Wells, Paul Banford, HGF Limited and Bioscience IP Limited have no equity interest in Evgen or the Company and this report is prepared in our capacity as independent consultants.

2. AN OUTLINE OF THE INTELLECTUAL PROPERTY REGISTRATION SYSTEMS RELEVANT TO EVGEN

2.1 THE PATENT SYSTEM

A patent confers a monopoly right that may be used, by the owner of the patent, to prevent others commercially exploiting an invention. The intention underlying the grant of patents is to reward those who innovate and who are also prepared to share their technology with the public. This is achieved by granting a monopoly for a limited period of time (normally 20 years – see below) in return for publishing the invention in a clear and complete manner in the form of a published patent specification. When the monopoly has expired the public has the benefit of being able to exploit the technology defined in the specification.

2.1.1 Patentability

The extent of a monopoly granted to an applicant is limited by the need to fulfill the requirements for patentability defined by the laws of the country in which patent protection is to be pursued. An applicant defines his monopoly in a single sentence known as a claim. A patent office examiner will decide whether or not the scope of a claim, submitted with a patent application, is allowable under the applicable law. The requirements for patentability do vary from jurisdiction to jurisdiction. However there are a number of common requirements that are worth highlighting and these are detailed below.

2.1.1.1 Novelty

A patent will only be granted if the invention claimed by an applicant is new. In most jurisdictions, a patent claim will lack novelty if subject matter falling within the definition of the applicant's claim has been disclosed, by the inventor or by any third party, prior to the filing of the application for the patent.

Most countries in the world require absolute novelty in view of any public disclosure that has been made before an applicant applies for patent protection. However some countries do allow a ''grace period'' whereby an inventor may still validly file for patent protection after they have disclosed their invention themselves. Furthermore a smaller number of countries, and notably the United States of America, have operated a ''first-to-invent'' system. This has meant that certain publications made before a patent is filed may not be held to be relevant if an applicant can prove the invention was made and reduced to practice prior to the earlier publication.

2.1.1.2 Inventive Step

Any claim that defines novel subject matter must also be considered by a patent office to define an ''inventive step.'' For a claim to be inventive it must be non-obvious or surprising to a person of ordinary skill in the relevant art at the date the patent application is filed.

2.1.1.3 Industrial Utility and Statutory Bars

The claims of a patent application must be useful in an industrial sense and must also not be excluded from protection by the laws of the jurisdiction in question.

In the United Kingdom, as-well-as other members of the European Patent Convention (''EPC''), there are a number of statutory bars (e.g. relating to methods of medical treatment) that, at least superficially, would appear to restrict patent protection in many of the technical areas of interest to Evgen. However patent office practice, and case law decided in the courts and patent offices, has evolved such that the restrictive effect of these bars is construed narrowly. Accordingly worthwhile patent protection may still be obtainable in Europe and we understand that Evgen has commercial interests in such technical areas (see below).

2.1.1.4 Sufficiency of Disclosure

It is a further requirement of patent laws that a patent specification, as originally filed, describes the claimed subject matter in a way that is clear, concise and would be sufficient to enable one of ordinary skill in the art to be able to carry out the invention. Therefore, if the invention is not fully disclosed, a patent office may refuse a patent application for lack of sufficiency.

2.1.1.5 Support

The patent systems of the world usually also require a patent specification to include at least some supporting data. This data is required to convince a patent examiner that the applicant has reduced the invention to practice across the full scope of the claim.

2.1.2 Patent Procedure

An applicant must carefully co-ordinate a patent filing programme in order that they may secure protection in each and every country in which protection is required.

2.1.2.1 Establishing a Priority Date

Applicants may take advantage of an International treaty (the Convention of Paris for the Protection of Industrialised Property – ''the Paris Convention'') that enables the applicant to file a single initial application in a state that is party to the Paris Convention. Most industrialized countries are party to this convention. The applicant then has a further period of time, after the initial filing date, to decide in which further Paris Convention states they will require patent protection. Under the Paris Convention a member state will recognize the priority date established by the first filed application provided that national filing requirements are met within a 12 month period from the filing of the first application.

2.1.2.2 Patent Applications claiming priority under the Paris Convention

As the 12 month anniversary approaches an applicant may decide to file patent applications in each and every national jurisdiction that may be of commercial interest. However this tactic has a number of disadvantages. One of the main disadvantages is that national filing costs (which can be considerable if global protection is required) will be incurred at this early stage in the procedure. Accordingly, most applicants elect to follow a procedure by which an international application is filed under the Patent Co-operation Treaty (''PCT'').

The PCT system allows an applicant to file a single international application that will cover a high proportion of the countries party to the Paris Convention and virtually all of the industrialised countries of the world. The PCT procedure can be followed for at least 30 months from the initial priority date for each of the designated states. However care needs to be taken at the 12 months stage to ensure that due consideration has been given to the requirement to file national phase applications in those few countries that are not members of the PCT. We understand that, to date, Evgen has not been interested in pursuing patent protection in non-PCT states.

PCT procedure is divided into two parts known as Chapter I and Chapter II of the PCT. Chapter I procedure is compulsory whereas Chapter II, as discussed below, is optional.

Under Chapter I, the international authorities issue an International Search Report (''ISR'') with an accompanying opinion on patentability. This enables an applicant to review the search results and opinion and come to a view as to whether or not their application defines novel and inventive subject matter. This information can then be used to adjust their patent strategy as appropriate.

Another part of the international procedure (and also the procedure for any national application) is that the patent specification is published around 18 months from the priority date. This publication date is important because it is the first opportunity for third parties to become aware of the contents of a patent application (prosecution files are kept secret until at least this date). This publication is generally known as an ''A Publication''.

Once an applicant has reviewed the ISR and opinion, he may choose to request a substantive examination (''Chapter II Examination'') and thereby enter Chapter II of the PCT. This procedure allows an applicant to enter into at least one round of prosecution with an International Examiner and will be terminated when the Examiner issues a final report on patentability. This report is known as the International Preliminary Report on Patentability (''IPRP'').

Following Chapter II Examination incurs extra cost and, in any event, is non-binding on future prosecution before national patent offices. It is therefore often the case that applicants decide to refrain from entering the Chapter II procedure. In this case an IPRP is still issued at the end of the international procedure and is based on the opinion on patentability that was issued with the ISR.

The ISR is published with the patent specification at the 18 month stage or, if the ISR is not prepared in time, as-soon-as possible thereafter. Opinions are not made available to the public although the IPRP is available when national phase prosecution begins (at 30 months from the priority date). This represents another important date because a third party will only be able to get any detailed insight on the International Authority's views of the patentability of an application after 30 months have elapsed from the filing of the first priority application.

2.1.2.3 National and Regional Prosecution of Applications Derived from International Applications

After 30 months have elapsed from the claimed priority date of an International Application, an applicant must file further applications in each and every state that is party to the PCT and in which national rights are required.

At this stage a number of separate applications are usually filed and this set of applications (all claiming priority from the initial priority application) are normally referred to as a ''patent family.'' Careful consideration needs to be given when choosing in which states to proceed because in most countries there are strict time limits (normally at 30 months from priority or shortly thereafter) by which national formalities must be completed. An applicant will incur significant costs at this stage if patent protection is required in many jurisdictions and it is therefore important to balance the conflicting pressures of budget management with the need to maximize patent protection in jurisdictions of commercial interest.

The applications comprising the patent family are prosecuted separately and according to national and regional laws until they give rise to granted patents. Most patent offices proceed to publish the granted form of the patent. This publication is commonly known as the ''B Publication''.

2.1.2.3.1 European Patent Applications

Usually a patent is granted, and is effective, in a given country following a patent application filed in that country and subsequent prosecution before the relevant national patent office. An important exception is where an application is filed at the European Patent Office (''EPO''), which designates one or more countries party to the EPC. Much like a PCT application, a European patent application is prosecuted before a single authority (the EPO) but may cover a number of European countries. The exact number of states coved by a European application depends upon which states were party to the EPC on the date of filing of the PCT application. The EPC currently covers the European Union and many economically important states that border the European Union.

If prosecution of a European application is successful, it will give rise to granted European rights. However these rights are not enforceable unless formal steps are taken to secure national patents in each designated country that is of interest to the applicant. Once these formalities are completed the patentee will be in possession of individual national patents that may be enforced separately through the relevant national courts. Patentees can incur significant costs at this stage in European procedure.

The EU is in the process of introducing a community patent that will have a significant impact on the way patents are made effective, and used, in EU countries. These changes are expected to take effect within a few years. However at the date of this report, it is not clear when these changes will come into force and we have not dwelt on the implications of a community patent for this report. Evgen will of course need to take advice and adapt it's IP strategy when the community patent arrives.

2.1.2.3.2 National Patent Applications

Post-PCT prosecution can be complex and, if protection is required in many countries, will involve multiple lines of prosecution. The national laws and procedures in each jurisdiction vary from country to country and it is therefore advisable, and usually mandatory, that agents qualified to act in a particular country represent a patentee's interests.

Accordingly patent families tend to be managed by a single attorney firm that has a direct relationship with the applicant. This attorney will then instruct other lawyers (competent to act in their own jurisdictions) to represent an applicant's interests at a national level.

2.1.3 Renewal of Patents and Patent Applications.

In addition to the normal procedure for the prosecution of patent applications, a patentee must also ensure any renewal fees are paid that are required to maintain patent applications and granted patents in force. Renewal fees must generally be paid annually although requirements do vary from country to country. This task can represent a significant administrative and cost burden for large patent portfolios.

2.1.4 Patent Term

The term of a patent is generally up to 20 years providing that any renewal fees necessary to maintain the patent in force are paid in due time. The term is calculated from the application date in most countries (normally corresponding to the PCT filing date).

The term of a patent can be extended if it protects a drug that has had to fulfill regulatory requirements (e.g. before the FDA or EMEA) before it can be protected. In most cases the patent term may be extended to up to a total of 25 years and such supplementary protection may be applied for after a marketing authorisation has been secured. The issues relating to patent term extension can be complex and a patentee should always seek advice from an attorney with experience in this field.

2.1.5 Rights in a Patent

The right to enforce a patent against a third party exists as from the date of grant. We do not propose to discuss procedures involved in an infringement action in any detail for the purposes of this report.

2.1.6 Post Grant Challenges to Validity

Once a patent has been granted, it is not immune from challenge. The validity of patents can be called into question either in specific proceedings for that purpose or as a counter claim as part of an infringement action undertaken against a third party.

2.1.7 Opposition Procedure

Many countries include an opposition procedure in the patent process whereby a third party may object to the grant of a patent. For instance, for nine months following the grant of a European patent, there is an opportunity for third parties to file an opposition against a European patent at the EPO.

2.2 THE TRADE MARK REGISTRATION SYSTEM

Registration of a trade mark in a territory provides the proprietor with an exclusive right to use their mark for the goods or services specified in the registration and entitles the owner to prevent third parties using an identical or confusingly similar mark.

Initially, a trade mark registration gives protection for a limited period, generally ten years, but thereafter the trade mark is renewable. Unlike the patent system there is no limit on the period of protection, and registrations can therefore be renewed *ad infinitum*. Thus when a patent for a product expires, if the owner has built up a sufficient reputation under the brand in the product, then public recognition of the brand may enable the owner to retain a good market share in the relevant product sector due to brand loyalty. It is possible to accrue rights in a trade mark without registration by virtue of use, but such rights are harder to establish and enforce. Where a registered trade mark is not used for a certain period, then the registration may become vulnerable to revocation should a third party attack the registration.

2.2.1 Registrability

A trade mark may consist of words, slogans or logos, and can include the form of packaging used for a product. A trade mark should only be registered if it has some distinctive character and fulfils the function of identifying the owner's goods and thereby indicates the origin of the goods to the buying public. A trade mark may be registered in relation to a specific listing of goods or services

and should rely upon actual use of the mark by the owner in relation to those goods or a genuine intention to use the mark in the territory concerned (although some jurisdictions, notably the EU, do not require an intent to use).

2.2.2 Protection in the European Union and the US

It is important to note that the problem of prior disclosure, which has a significant impact on patentability and therefore places strict time constraints on when patent applications may be filed, is not relevant to the registrability of a trade mark. Accordingly a business seeking to protect a brand can choose to do so in a staggered way and there can often be several years between the first filing and the filing of trade mark applications in secondary markets.

A business usually elects to secure trade mark protection in their home markets. Thus a UK-based business usually begins a trade mark registration programme by filing before the UK Intellectual Property Office. The next step is often to expand rights throughout Europe and also to cover the USA.

In Europe there is a European Community Trade Mark System (''CTM'') which enables trade mark owners to secure registered protection for their trade marks throughout all member countries of the European Union. The system represents a cost effective way of securing European-wide rights.

In the United States registration can be achieved by filing an application either on the basis of an intention to use the mark in commerce in the US; on the basis of actual use of the trade mark in the US; or on the basis of a ''home'' registration. Due to the significant lead-in period for pharmaceutical products, the strategy for pharma/life science businesses is often to secure protection for the marks of interest in the UK or the EU and use them to support their applications in the US. The US system also provides that once a mark has been registered for a period of five to six years the owner must file an affidavit of use to satisfy the US Patent and Trademark Office that he is entitled to continued protection for the brand.

Elsewhere, it is possible to obtain national trade mark protection in countries of interest. Businesses in the pharma fields may wish to establish a large trade mark portfolio prior to securing a market authorisation (especially if significant effort is being invested in the brand). However companies do have the option to defer filing for global protection until clinical trials and/or an application for a market authorisation are more advanced.

2.2.3 Renewal of Trade Marks

Timely payment of renewal fees is required to maintain trade mark registrations. Trade mark registrations fall due for renewal periodically – the period for the UK and the US is every ten years.

2.2.4 Trade Mark Term

The term of a registration is usually ten years, and providing that any renewal fees and necessary affidavits of use are filed and paid on time, a trade mark may be renewed indefinitely.

2.2.5 Challenges to Validity

A trade mark is also not immune from challenge when it has been registered. A trade mark may be attacked on the basis that the mark has not been used or on the basis that the mark has become generic, misleading or deceptive. A trade mark registration may also be declared invalid on the basis that it should never have been registered, for example because it was not sufficiently distinctive to function as a trade mark, or because there was a prior existing registration.

2.2.6.1 Opposition Procedure

In the UK and the US and most other territories where trade mark protection is possible, there is a procedure for opposition to a trade mark application. Generally there is publication of the trade mark application and a statutory period during which third parties may oppose (on the basis of a prior right or on the basis that the mark should not be registered for other reasons).

2.2.6.2 Revocation and Invalidity Proceedings

It is generally possible to apply for revocation of a trade mark in a country where the mark has not been used for a specified period. In the UK this period is five years, although it varies from country to country.

It is also possible to apply for invalidity of a trade mark on the basis that it should never have been registered, such that it was, for example, not sufficiently distinctive to function as a trade mark or where there was a prior existing right and the owner had perhaps missed the opportunity to oppose.

Revocation may also be sought if a trade mark has become generic or is deceptive.

2.3 OTHER INTELLECTUAL PROPERTY RIGHTS

It is also possible to file applications to register designs which generally protect the appearance of products. There are also a number of unregistered rights which include copyright, unregistered design rights and unregistered trade mark protection.

Such rights are usually of secondary importance to technology led businesses and more specifically we do not believe these rights are of particular relevance to Evgen at this stage in the development of a stabilised sulforaphane (''sSFN'') product.

This report therefore primarily focuses on the patents and to a lesser extent the trade marks upon which Evgen relies.

2.4 REGULATORY DATA EXCLUSIVITY

Securing market approval for a pharmaceutical product also allows the market authorisation holder to benefit from a period of regulatory data exclusivity that is granted to an innovating company following a first marketing authorisation for a product.

The term of such exclusivity varies from country to country but is typically available for 5-10 years after a marketing authorisation has been granted. This data exclusivity is important because generics companies are not allowed to rely upon the data submitted to regulatory authorities by the innovator until after the exclusivity period has expired. This means they would have to replicate all of the submitted safety and efficacy data if they were to seek their own marketing authorisation and, for all intents and purposes, this represents a significant barrier to the market for such generics companies. Accordingly generics companies tend to wait for the patents and the data exclusivity period to expire before marketing a competing product.

Data exclusivity is not strictly considered as an IP right. However it is clearly very relevant to the monopoly a business can rely upon for a pharmaceutical product and is an important parallel right to patents. It is sometimes the case that patents will expire before the data exclusivity period or adequate patent rights may not even exist. When this is the case, data exclusivity can be the main defense against competing products.

3. THE IP STRATEGY OF EVGEN

We are satisfied that the management of the Company is well aware of the importance of IP to a technology based company.

We understand that IP strategy is given serious consideration at Board level. This is evidenced by the fact that Bioscience IP Limited was commissioned to conduct a review of Evgen's IP strategy for its SULFORADEX® technology and lead product (SFX-01) in February 2012. Bioscience IP Limited also conducted a patent landscaping exercise in April 2012 (see our comments in Section 6.1 below).

The Board of Evgen delegates day-to-day management of the patent portfolio and issues relating to freedom-to-operate to the Chief Executive Officer (''CEO''). It is clear that the CEO has significant experience in the management of IP and in particular knows when it is appropriate to seek professional advice from qualified Chartered and European Patent Attorneys and other legally qualified professionals. General IP counsel is provided by Paul Banford through Bioscience IP Limited whereas HGF and Sally Cooper manage the patent and trade mark portfolios respectively.

As part of the Company's general policy we are informed that all people who work for, or visit, Evgen are aware that scientific developments are the confidential property of Evgen and that such developments must remain secret prior to the filing of patent applications and ideally for the first 18 months of the life of a patent application.

3.1 Patent Strategy

Evgen's main strategy has been to enter into agreements with patent holders to secure rights in patents that are relevant to the manufacture and use of sulforaphane-cyclodextrin complexes. To

date Evgen has acquired an exclusive licence, or an option to an exclusive licence, to a portfolio of four patent families (see Section 5 below). Furthermore, by agreement, Evgen controls the prosecution of these patent families. They are managed by HGF. We believe this licensing programme has allowed Evgen to gain access to patent families that define monopolies around its key technologies and it is pleasing to note that the licence arrangements include options to take assignment of relevant patent and patent applications (see below).

Evgen also creates Invention Disclosure Records in respect of any research and development (whether in-house, through contract services or through collaboration agreements) that may be capable of attracting patent protection. Evgen reviews these records and contacts a patent attorney to discuss patentability and a filing strategy for any developments that Evgen feel may have commercial significance.

3.1.1. Before an application is filed

Invention Disclosure Forms are currently filled out by, or communicated to, the CEO.

The CEO and a patent attorney from Bioscience IP or HGF will then make a preliminary review of the patentability of the subject matter and may, if appropriate, also conduct some prior art searches. The extent of the review and any searches is dictated by a number of factors including the commercial importance of the technology and also Evgen's prior knowledge of the subject area.

A decision is then made by the CEO whether or not a patent application should be prepared. If an application is required, HGF is provided with a technical summary and will proceed to prepare a patent specification. A priority application is filed once the specification has been approved by Evgen.

3.1.2 Initial Filing

To date, and for sound procedural reasons, Evgen has arranged for priority applications to be filed before the USPTO, but will also file before the UKIPO and other national/regional offices as appropriate. HGF make recommendations to Evgen when making a decision with regards filing priority applications in additional or alternative jurisdictions.

Evgen decides whether or not a search should be conducted by a patent office during the priority year. This decision is also influenced by commercial and patent tactics as-well-as whether or not the patent office chosen for the priority application offers the possibility of commissioning a search in the priority year.

3.1.3 International Prosecution

Evgen routinely files a PCT application within 12 months of the filing of the priority application. Once a priority claim has been made the initial priority application is usually allowed to lapse and future patent protection based on the subject matter defined in the PCT specification.

3.1.4 National and Regional Phase Prosecution

As the deadline for filing national and regional applications approaches (30 months from the priority date), HGF discusses with Evgen what national filing strategy may be required.

There are well over 100 countries that are signatories to the PCT and, for budgetary reasons, it is necessary for Evgen to secure optimal market coverage whilst being pragmatic with regards the number of countries in which it proceeds to seek protection. To date, and where Evgen has had control of the patent application process, Evgen has chosen to file patent applications in at least Australia, Canada, China, Japan, USA and Europe (designating all the main contracting states) for any technology that is directly relevant to the development of a SULFORADEX® product. This strategy has evolved and should continue to evolve as the development of products advances. We are satisfied that Evgen appreciate the importance of the selection procedure at this stage and HGF believes Evgen has to date adopted a good strategy.

3.2 Trade Mark Strategy

Evgen, to date, has adopted the strategy of protecting the main SULFORADEX® trade mark in two major markets (Europe and the USA).

Unlike with patents, trade mark applications can generally be made in response to a commercial imperative. We therefore understand that Evgen will give consideration to extending the territorial

protection for the brand and also to selecting and registering additional individual product brands when it changes or expands its marketing strategy.

If Evgen proceed with registering individual product brands then they should ensure that trade mark searches are conducted prior to adoption of any such trade mark to ensure that they are not infringing any existing rights. Thereafter, if the mark appears to be available for use and registration, applications should be filed to protect the trade mark in the territories of interest, presumably at least in Europe and the USA, but also consideration should be given to seeking protection in other potentially important markets.

3.3 Renewals Procedures

Evgen uses HGF's renewals service to deal with patent renewal fees. HGF are instructed to pay all renewals by default and payment should only be omitted in view of specific instructions to refrain from paying. We consider this to be an appropriate and safe approach to renewal of patent rights.

Trade marks renewal fees generally fall every 10 years and, given that Evgen's trade marks are less than 10 years old (see below), no renewals have fallen due to date. We understand that Evgen will instruct Sally Cooper to deal with renewals as they arise.

4. AN OVERVIEW OF THE PROPRIETARY TECHNOLOGY RELIED UPON BY THE COMPANY

The Company's primary interest is in the development of stable, clinically useful sulforaphane for use in the treatment of human disease and in particular in the prevention or treatment of cancers and neurodegenerative disease, initially subarachnoid haemorrhage.

A number of medical benefits associated with isothiocyanates, such as sulforaphane, are well known in the scientific literature. However, to date, it has not been possible to exploit these molecules in the form of a pharmaceutical product because isothiocyanates are very unstable and it has not been possible to formulate a product that has a viable shelf-life.

Evgen has recognised that the stability of isothiocyanates represents a significant problem to the pharmaceutical industry and has therefore initiated a research and development programme with the ultimate aim of providing clinicians with stable isothiocyanates that retain bioactivity.

A key area of development has been in association with PharmAgra Labs Inc (''PharmAgra''). PharmAgra has managed to produce stabilised sulforaphanes (''sSFNs'') by complexing sulforaphane with a cyclodextrin. PharmAgra filed for patent protection (establishing a priority date in 2007) and Evgen has secured an exclusive licence to enable it to develop a pharmaceutical product based on the PharmAgra technology. This patent family can be viewed as the ''master'' or ''foundation'' patent supporting Evgen's commercial aims and is discussed in more detail in Section 5.1.2 below. Evgen's agreement with PharmAgra provides a pipeline for access to further technological developments made at PharmAgra and two further patent applications have been filed based on such technologies discussed at Sections 5.1.3 and 5.1.4 below.

SULFORADEX® is the brand name that is currently being used by the Company in association with the technology that enables a stable cyclodextrin-sulforaphane complex to be formed for use in pharmaceutical markets. The lead product is SFX-01 and this is manufactured under contract by PharmAgra.

We understand that primary areas of interest for the Company are in developing a pharmaceutical product for oral consumption, which comprises the SFX-01 product, for treating breast cancer and subarachnoid haemorrhaging. However the use of sSFNs (more broadly) in the treatment of a wider range of conditions and diseases (including advanced cancers as part of a combination therapy) is being actively investigated.

It is of primary importance that the Company develops an IP portfolio that at least defines a monopoly around the SFX-01 product and its use for treating conditions of primary interest. However the Company has recognised that it would also be desirable to protect the broader ''space'' around its commercial interests and seek to secure IP protection for any sSFN for treating any medical condition.

Evgen has also entered into a Licence Option Agreement with Consejo Superior de Investigaciones Cientificas (CSIC) and Universidad de Sevilla in connection with sulforaphane analogues that are defined in the patent family discussed in section 5.2 below. Such analogues have the potential to give rise to alternative or complementary products to those based on sulforaphane *per se.* Under

the terms of the agreement Evgen is evaluating the efficacy of the analogues and, should the analogues be of interest to Evgen, it has the exclusive right to negotiate a commercial licence. HGF, under Evgen's instructions (and as agreed by the parties to the agreement), is managing the prosecution of the patent applications.

5. THE STATUS OF THE PATENT AND TRADE MARK RIGHTS UPON WHICH THE COMPANY RELIES.

The Company currently relies upon the following IP:

(i) a patent portfolio exclusively licenced from PharmAgra (outlined in Section 5.1 below);

(ii) an option to license a patent family filed in the name of Consejo Superior de Investigaciones Cientificas (CSIC) and Universidad de Sevilla (outlined in Section 5.2 below);

(iii) a pipeline of technology that is likely to give rise to further patent applications (outlined in Sections 5.1.1 and 5.3 below); and

(iv) Evgen's own trade marks (outlined in Section 5.4 below).

5.1 IP LICENSED FROM PHARMAGRA

5.1.1 Terms of the PharmAgra Licence

Evgen has entered into an exclusive licence agreement with PharmAgra (and co-assignees Lalilab Inc) which permits Evgen to exploit the technology outlined in the patent families discussed in this Section 5.1 within a field of use covering pharmaceuticals and all prescription medicaments (other than those for topical use) that comprise sulforaphane stabilised with cyclodextrin.

The patent family discussed at Section 5.1.2 below represented background intellectual property that was licensed when the PharmaAgra Agreement was executed.

The PharmAgra licence also requires the licensors to deposit with Evgen all their know-how (within the field of the licence) and for both parties to notify any improvements each to the other. These provisions have allowed Evgen to review developments at PharmAgra and arrange for further patent applications to be filed (discussed at 5.1.3 and 5.1.4 below). This pipeline is a useful resource for Evgen and provides for the possibility for Evgen to pursue patent protection for any further inventions (whether invented by PharmAgra, Evgen or jointly) that are made in the future.

Under the terms of the PharmaAgra Agreement, Evgen is responsible for managing the prosecution of the relevant PharmAgra patents. There is also an option for relevant patent rights to be assigned to Evgen.

HGF is handling the prosecution of these patent families under Evgen's instructions.

5.1.2 THE PATENT FAMILY COVERING SULFORADEX® *per se*

This patent family concerns the stabilisation of sulforaphane, or an analogue thereof, by forming a complex between the sulforaphane, or an analogue thereof, and a cyclodextrin. The patent specification also defines methods of preparing sulforaphane-cyclodextrin complexes and also claims such complexes *per se*.

Cyclodextrin is well known as a stabilising agent in the pharmaceutical industry for hydrophobic molecules. However the patent specification explains that sulforaphane is a hydrophilic molecule and as such a skilled person would have expected a complex of sulforaphane and cyclodextrin to be more soluble in water than cyclodextrin alone. Accordingly the state of the art was that a skilled person would have expected to be unable to isolate a complex from a solution containing free cyclodextrin and would therefore not have contemplated stabilising sulforaphane with cyclodextrin. However the inventors found, to their surprise, that the complex was in fact less soluble and they were able to isolate sSFN. This section of the specification was used to support arguments in favour of an inventive step in jurisdictions such as the US and it remains to be seen if this argument can be used to support an inventive step in jurisdictions where applications are still pending (see section 5.1.2.2 below).

5.1.2.1 Summary of Patent Procedure to date

Priority date: 23 January 2007

US and International filing dates: 23 January 2008

Country	Application No.	Grant No.	Status
Australia	200820953	200820953 B	GRANTED
Canada	2,672,971	2,672,971	GRANTED
Europe	EP14166888.9	N/A	PENDING – await examination report
Japan	2013-210752	N/A	PENDING – await next Office Action
USA	US 12/009,874	US 7,879,822	GRANTED

Inventors: Ido Dov Dagan
Albert Roger Frisbee
Peter Wyatt Newsome
Michel Pierre Baudet

Owner: Pharmagra Labs Inc.

International Patent Application Number PCT/US2008/000832 claimed priority from US 60/881,875 and was published on 31 July 2008 as WO 2008/091608. National phase applications were filed in Australia, Canada, Europe and Japan when the international procedure terminated. US 12/009,874 was not derived from the International application but was filed at the same time as the PCT application and also claims priority from US 60/881,875.

5.1.2.2 Summary of the Rights conferred by this Patent Family

PharmAgra has secured granted patents in Australia, Canada and the USA and has pending applications in Europe, Hong Kong and Japan.

Protection in the USA

The independent claims of US 7,879,822:

1. A method of stabilizing sulforaphane, or an analog thereof, the method comprising:
contacting sulforaphane or an analog of sulforaphane selected from one or more of [*10 isothiocyanates*] and mixtures thereof, and at least one cyclodextrin to form a complex between the sulforaphane, or analog of sulforaphane, and the at least one cyclodextrin.

20. A composition comprising a complex of sulforaphane and a cyclodextrin.

24. A pharmaceutical composition comprising a complex of cyclodextrin and sulforaphane, or an analog of sulforaphane selected from the group consisting of [*10 isothiocyanates*] and mixtures thereof, and an excipient.

29. A nutraceutical composition comprising a complex of cyclodextrin and sulforaphane, or an analog of sulforaphane selected from the group consisting of [*10 isothiocyanates*] and mixtures thereof, and an excipient.

Dependent claims specify that the cyclodextrin may be a W6, W7 or W8 cyclodextrin.

Claims 24 and 29 broadly cover pharmaceutical and nutraceutical compositions comprising any one of 11 isothiocyanates (sulforaphane and 10 analogs) and combinations thereof complexed with a cyclodextrin. We believe the term cyclodextrin used in the independent claims should be construed to mean any cyclodextrin because of the repercussive effect of the dependent claims which specify that the cyclodextrin may be one of three specific cyclodextrins. These claims appear to represent valuable protection for Evgen because claims to pharmaceutical and nutraceutical compositions *per se* can be used to prevent third parties from possessing and using such compositions for any commercial purpose (i.e. irrespective of the medical indication for such compositions).

It should be noted that claim 20 is broader than claims 24 and 29 insofar as it defines any composition (i.e. not just a pharmaceutical or nutraceutical) but is narrower in other respects because it only encompasses sulforaphane and not analogs thereof.

Claim 1 is also important to Evgen because it prevents third parties from stabilising any one of 11 isothiocyanates (sulforaphane and 10 analogs) and combinations thereof by complexing with a cyclodextrin. The scope of protection is not limited by the ultimate use of the stabilised sulforaphane. The claim appears to encompass any way of complexing with a cyclodextrin that

results in stabilisation of sulforaphane and as such represents a valuable patent that can be asserted against any third party wishing to stabilise sulforaphane with cyclodextrin.

It is our view that this patent is very important for protecting Evgen's commercial aims in the US. This is because at least claims 20 and 24 define and protect the SULFORADEX® product and claim 1 very broadly protects methods of making such a product.

Any formal opinion on the scope of the US claims should be obtained from a US patent attorney. However, it is HGF's view that this granted patent will be the single most important patent that will protect Evgen's interests (as exclusive licensee) in the US.

HGF was not responsible for the prosecution of the US application and we have not made a detailed review of the file history for the purposes of this report. However, following a brief review, it appears that the US attorney pursued protection with all due diligence and successfully convinced the Examiner to allow broad protection for this technology. PharmAgra's attorney successfully argued that it was not obvious to combine sulforaphane and cyclodextrin. The USPTO's main argument was that FR 2,888,235 (a French patent in the name of Nutrinov) rendered claims obvious. However PharmAgra was able to ''swear behind'' this document with the effect that it was not citable in the US (even though it was published before the priority date for this application). This was possible because US patent law was based on a ''first-to-invent'' system. PharmAgra were able to successfully argue that the document should not be considered under US procedure because they submitted a sworn statement that their inventors reduced the invention to practice before the publication date of FR 2,888,235.

HGF believes the US patent will be very useful for defending the US market-place and the exclusive licence from PharmAgra therefore represents a very valuable IP asset.

Protection in Europe

The pending application (EP14166888.9) is a divisional patent application based on EP08724719.3 (the original ex-PCT application filed at the end of the international procedure). The application published as EP 2796140 A on 29 October 2014 and the following claims are currently pending:

1. A method of stabilizing sulforaphane, the method comprising:

   contacting sulforaphane and at least one cyclodextrin to form a complex between the sulforaphane and the at least one cyclodextrin

   wherein the step of contacting sulforaphane and at least one cyclodextrin comprises:

   adding sulforaphane to a saturated solution of the cyclodextrin in water; and separating the complex from the solution.

2. A method according to Claim 1, wherein the complex is separated from the solution by precipitation.

3. A method according to Claim 2, wherein the precipitation is collected by filtration.

4. A method according to Claims 1 to 3, wherein the collected precipitate is dried to a constant weight under vacuum.

5. A method according to Claim 1, wherein the complex is collected as a precipitate, and is optionally urged to precipitate by cooling at -4°C, wherein said precipitate is collected by filtration, and is then dried to a constant weight under vacuum.

6. A method according to any proceeding Claim, wherein the at least one cyclodextrin is selected from the group consisting of W6 (alpha) cyclodextrin, W7 (beta) cyclodextrin, W8 (gamma) cyclodextrin, and mixtures thereof.

7. A complex of sulforaphane and a cyclodextrin obtainable by a method as defined in any one of claims 1 to 6.

8. A pharmaceutical composition or a nutraceutical composition comprising the complex of claim 7 and an excipient.

9. A composition according to Claim 8 wherein the composition is for administration by one or more of oral, topical, parenteral, injectable, buccal, sublingual, intramuscular, or intravenous routes.

10. A composition according to Claim 9, wherein the composition is an oral dose form and is one or more of a dietary supplement, a food product, a food supplement, or a food additive.

11. A composition according to Claim 9, wherein the composition is a topical dose form and is one or more of a cream, jelly, ointment, or suspension

These claims were filed in response to objections set out in a Written Opinion of the Search Division.

A partial search report was generated by the EPO that focused on complexes comprising sulforaphane *per se*. The Search Examiner argued that further search fees would need to be paid if sulforaphane analogues were to be considered. Evgen decided to refrain from contesting this finding and did not pay any further search fees. This was because Evgen is content for prosecution to focus on the complex which is the main focus of its commercial interests (i.e. sSFN *per se*). Furthermore it will be possible to file a divisional application(s) at a future date if Evgen wish to pursue protection for the analogues of sulforaphane. HGF believes this is a good strategy.

A formal Search Report and Written Opinion (based on sSFN) was subsequently prepared by the Examiner and issued in November 2014. The Examiner raised objections similar to those raised for the parent case (EP08724719.3 – see below) and, in response, HGF filed the current claims with new arguments in support of patentability in June 2015. The new arguments presented in June 2015 focused on the fact that the particular process defined in the new claim 1 is not disclosed in the prior art and that this particular process gives rise to sulforaphane-cyclodextrin complexes with higher loadings of sulforaphane. Pending claim 7 seeks protection for the sulforaphane-cyclodextrin complexes that are the product of this process and pending claims 8 to 11 relate to pharmaceutical compositions comprising these complexes. The application will now be passed to the Examining Division and Evgen is currently waiting for a substantive Examiner to express a view on the patentability of the pending claims.

EP08724719.3 (the application from which the pending divisional application is derived) faced a number of objections in view of prior art that included FR 2,888,235 (the document that was not citable in the US). FR 2,888,235 primarily discloses the extraction of sulforaphane from botanical sources using unrelated technology. However a single sentence in the specification discloses that ''several encapsulation supports can also be used [with sulforaphane], such as maltodextrins, cyclodextrins''. Despite the speculative nature of this disclosure the European Examiner has argued that this statement suggests it would be obvious to combine cyclodextrin with sulforaphane as defined by claims filed with EP08724719.3. A number of claim amendments were filed by the previous attorneys and subsequently by HGF for consideration by the Examiner. However the Examiner would not accept these amendments defined inventive subject matter and summoned the applicant to oral proceedings to present arguments in person. HGF was, and remains, of the view that good arguments could have been presented at oral proceedings to support an inventive step for the claims placed on file before the summons was made. Nevertheless a strategic decision was made to file a divisional application (EP14166888.9) and withdraw EP08724719.3. At least one reason for doing this was that Evgen wanted to keep its options open (insofar as scope of protection is concerned) while SULFORADEX® is being developed and a pending divisional application with relatively broad claims was considered the best strategy.

HGF believes that it should be possible to secure some worthwhile protection in Europe and this view is supported by the fact that patent protection has been secured in Australia and Canada (jurisdictions where FR 2,888,235 was also citable).

Nevertheless, in the worst case scenario, Evgen may only be able to secure narrow protection or even no protection in Europe. However, should this be the case, HGF is of the opinion that Evgen can still enjoy a strong market position on the basis of the regulatory data exclusivity provisions it should be able to rely upon in the EU and elsewhere (see 2.4 above).

HGF understands that sulforaphane has not been previously approved in Europe as a medicinal product for human or veterinary use. We also understand that, in order for Evgen to obtain a marketing authorisation in Europe, it will be necessary to prepare a full regulatory dossier to establish the safety and efficacy of this product. Under these circumstances, sSFN should be entitled to regulatory data exclusivity in Europe under the provisions of EU Directive 2004/27/EC (amending Directive 2001/83/EC).The likely data exclusivity term in Europe for a SULFORADEX® product should run for 10 years from the date of European marketing approval. We understand that market approval for a SULFORADEX® product is likely to be after 2018 and as such Evgen should be able to rely upon regulatory data exclusivity until at least 2028.

Protection in other Jurisdictions

Granted rights have been secured in Australia on the basis of the following claims:

1. A method of stabilizing sulforaphane, or an analog thereof, the method comprising:

   (a) contacting sulforaphane, or an analog thereof, and at least one cyclodextrin to form a complex between the sulforaphane, or analog thereof, and the at least one cyclodextrin,

   wherein the step of contacting sulforaphane, or an analog thereof and the at least one cyclodextrin comprises:

   dissolving or suspending at least one cyclodextrin in a solvent or mixture of solvents to form a solution or suspension; and

   dissolving or suspending sulforaphane, or an analog thereof, in the solution or suspension; and

   (b) separating the complex from the solution or suspension.

2. A method of stabilizing sulforaphane, or an analog thereof, the method comprising:

   (a) contacting sulforaphane, or an analog thereof, and at least one cyclodextrin to form a complex between the sulforaphane, or analog thereof, and the at least one cyclodextrin,

   wherein the step of contacting sulforaphane, or an analog thereof the at least one cyclodextrin comprises:

   dissolving or suspending sulforaphane, or an analog thereof, in a solvent or a mixture of solvents to form a solution or suspension; and

   dissolving or suspending at least one cyclodextrin in the solution or suspension; and

   (b) separating the complex from the solution or suspension.

3. A method of stabilizing sulforaphane, or an analog thereof, the method comprising:

   (a) contacting sulforaphane, or an analog thereof, and at least one cyclodextrin to form a complex between the sulforaphane, or analog thereof, and the at least one cyclodextrin,

   wherein the step of contacting sulforaphane, or an analog thereof the at least one cyclodextrin comprises:

   dissolving or suspending at least one cyclodextrin in a solvent or mixture of solvents to form a first solution or suspension,

   dissolving or suspending sulforaphane, or an analog thereof, in the same or different solvent or mixture of solvents to form a second solution or suspension; and

   combining the first solution or suspension with the second solution or suspension.

   (b) separating the complex from the solution or suspension.

4. A method according to any one of claims 1 to 3, wherein the at least one cyclodextrin is selected from the group consisting of W6 (alpha) cyclodextrin. W7 (beta) cyclodextrin. W8 (gamma) cyclodextrin, and mixtures thereof.

5. A method according to any one of Claims 1 to 4, wherein the analog of sulforaphane is selected from the group consisting of 6-isothiocyanato-2-hexanone, exo-2-acetyl-6-isothiocyanatonorbornane, exo-2-isothiocyanoat-6-methylsulfonylnorbornane, 6-isothiocyanato-2-hexanol, 1-isothiocyanato-4-dimethylphosphonylbutane, exo-2-(1'-hydroxyethyl)-5-isothiocyanatonorborane, exo-2-acetyl-5-isothiocyanoatonorbornane, 1-isothiocyanato-5 -methylsulfonylpentane, and cis-or tians-3-

   (methylsulfonyl)cyclohexylmethylisothiocyanate, and mixtures thereof.

6. A method according to any one of Claims 1 to 5, wherein the step of contacting sulforaphane, or an analog thereof, with at least one cyclodextrin to form a complex with cyclodextrin comprises contacting sufficient amounts of sulforaphane and a cyclodextrin to give a weight load of between about 0.01% wt/wt and about 30% wt/wt sulforaphane to cyclodextrin in the complex.

7. A method according to any one of claims 1 to 6, wherein the complex is separated from the solution or suspension by precipitation.

8. A method according to any one of claims 1 to 6, wherein the complex is separated from the solution or suspension by drying to a constant weight.

9. A method according to any one of claims 1 to 8, wherein the solvent or mixture of solvents used for dissolving or suspending at least one cyclodextrin comprises water.

10. A method according to any one of claims 1 to 8 wherein a single solvent is used for dissolving or suspending at least one cyclodextrin.

11. A method according to claim 10, wherein the solvent is water.

12. A complex of sulforaphane, or an analog thereof, and a cyclodextrin prepared according to any one of claims 1 to 11.

13. A composition comprising a complex according to claim 12.

14. A pharmaceutical or nutraceutical composition according to claim 13, comprising a complex of cyclodextrin and sulforaphane, or an analog of sulforaphane, and an excipient.

15. A composition according to Claim 13 or Claim 14, wherein the composition is administered in one or more of oral, topical, parenteral, injectable, buccal, sublingually, intramuscularly, or intravenously.

16. A method of stabilizing sulforaphane, or an analog thereof; or a composition comprising a complex of sulforaphane or an analog thereof and a cyclodextrin; or a pharmaceutical or nutraceutical composition comprising a complex of sulforaphane or an analog thereof and a cyclodextrin, substantially as herein described with reference to the Examples and/or Figures.

The three method claims (claims 1-3) allowed in Australia broadly cover the methods that may be employed to make sSFN and are supported by claims to the complexes made by such methods.

Granted rights have been secured in Canada on the basis of the following claims:

1. A method of stabilizing sulforaphane, or an analog thereof, the method comprising:

   contacting sulforaphane or an analog of sulforaphane and at least one cyclodextrin to form a complex between the sulforaphane, or analog of sulforaphane, and the at least one cyclodextrin;

   wherein the analog is selected from one or more of 6 isothiocyanato-2-hexanone, exo-2-acetyl-6-isothiocyanatonorbornane, exo-2-isothiocyanato-6-methylsulfonylnorbornane, 6-isothiocyanato-2-hexanol, 1-isothiocyanato-4-dimethylphosphonylbutane, exo-2-(1'-hydroxyethyl)-5-isothiocyanatonorborane, exo-2-acetyl-5-isothiocyanoatonorbornane, 1-isothiocyanato-5-methylsulfonylpentane, and cis- or trans-3-(methylsulfonyl)-cyclohexylmethyl-isothiocyanate, and mixtures thereof.

2. The method according to claim 1, wherein the at least one cyclodextrin is selected from the group consisting of W6 (alpha) cyclodextrin, W7 (beta) cyclodextrin, W8 (gamma) cyclodextrin, and mixtures thereof.

3. The method according to claim 1, wherein the step of contacting sulforaphane, or the analog thereof, and at least one cyclodextrin comprises:

   dissolving or suspending the at least one cyclodextrin in a solvent or mixture of solvents to form a solution or suspension; and

   dissolving or suspending the sulforaphane, or the analog thereof, in the solution or suspension.

4. The method according to claim 3, further comprising the step of separating the complex from the solution or suspension.

5. The method according to claim 1, wherein the step of contacting sulforaphane, or the analog thereof, and at least one cyclodextrin comprises:

   dissolving or suspending the sulforaphane, or the analog thereof, in a solvent or mixture of solvents to form a solution or suspension; and

   dissolving or suspending the at least one cyclodextrin in the solution or suspension.

6. The method according to claim 5, further comprising the step of separating the complex from the solution or suspension.

7. The method according to claim 1, wherein the step of contacting sulforaphane, or the analog thereof, with the at least one cyclodextrin to form a complex with cyclodextrin comprises contacting sufficient amounts of sulforaphane and a cyclodextrin to give a weight load of between about 0.01% wt/wt and about 30% wt/wt sulforaphane to cyclodextrin in the complex.

8. The method according to claim 1, wherein the step of contacting sulforaphane, or the analog thereof, and at least one cyclodextrin comprises:

   dissolving or suspending the at least one cyclodextrin in a solvent or mixture of solvents to form a first solution or suspension;

   dissolving or suspending the sulforaphane, or the analog thereof, in the same or different solvent or mixture of solvents to form a second solution or suspension; and

   combining the first solution or suspension with the second solution or suspension.

9. A complex of sulforaphane and a cyclodextrin.

10. The complex according to claim 9, wherein said cyclodextrin is selected from the group consisting of W6 (alpha) cyclodextrin, W7 (beta) cyclodextrin, W8 (gamma) cyclodextrin, and mixtures thereof.

11. A complex of an analog of sulforaphane and a cyclodextrin,

    wherein the analog is selected from one or more of 6 isothiocyanato-2-hexanone, exo-2-acetyl-6-isothiocyanatonorbornane, exo-2-isothiocyanato-6-methylsulfonylnorbornane, 6-isothiocyanato-2-hexanol, 1-isothiocyanato-4-dimethylphosphonylbutane, exo-2-(1'-hydroxyethyl)-5-isothiocyanatonorborane, exo-2-acetyl-5-isothiocyanoatonorbornane, 1-isothiocyanato-5-methylsulfonylpentane, and cis- or trans-3-(methylsulfonyl)-cyclohexylmethyl-isothiocyanate, and mixtures thereof.

12. A pharmaceutical composition comprising a complex of cyclodextrin, sulforaphane or an analog of sulforaphane, and an excipient,

    wherein the analog is selected from one or more of 6 isothiocyanato-2-hexanone, exo-2-acetyl-6-isothiocyanatonorbornane, exo-2-isothiocyanato-6-methylsulfonylnorbornane, 6-isothiocyanato-2-hexanol, 1-isothiocyanato-4-dimethylphosphonylbutane, exo-2-(1'-hydroxyethyl)-5-isothiocyanatonorborane, exo-2-acetyl-5-isothiocyanoatonorbornane, 1-isothiocyanato-5-methylsulfonylpentane, and cis- or trans-3-(methylsulfonyl)-cyclohexylmethyl-isothiocyanate, and mixtures thereof.

13. A nutraceutical composition comprising a complex of cyclodextrin, sulforaphane or an analog of sulforaphane, and an excipient,

    wherein the analog is selected from one or more of 6 isothiocyanato-2-hexanone, exo-2-acetyl-6-isothiocyanatonorbornane, exo-2-isothiocyanato-6-methylsulfonylnorbornane, 6-isothiocyanato-2-hexanol, 1-isothiocyanato-4-dimethylphosphonylbutane, exo-2-(1'-hydroxyethyl)-5-isothiocyanatonorborane, exo-2-acetyl-5-isothiocyanoatonorbornane, 1-isothiocyanato-5-methylsulfonylpentane, and cis- or trans-3-(methylsulfonyl)-cyclohexylmethyl-isothiocyanate, and mixtures thereof.

14. The composition according to Claim 13, wherein the composition is formulated for injection or for oral, topical, parenteral, buccal, sublingual, intramuscular or intravenous administration.

Protection in Canada mirrors the same broad protection allowed in the US.

Prosecution in Japan has followed a similar route to Europe and JP 2013-210752 is a divisional of the first Japanese application filed at the end of the international procedure. Evgen filed a response to a first Examination Report from the Japanese Patent Office in May 2015. The amendments and arguments presented to the Examiner followed the strategy for the European application discussed above. It is not possible to predict how prosecution will progress in Japan at this stage. However it is also worth noting that regulatory data exclusivity is also available for up to 8 years following a marketing authorisation in Japan.

Granted patents derived from PCT/US2008/000832 may be asserted against third party activity up until 23 January 2028 (provided renewal fees are paid in a timely manner and subject to any supplementary patent term that may be available).

In view of a patent term adjustment allowed by the USPTO, rights in US 7,879,822 may be asserted against third party activity up until 12^{h} November 2028 (provided renewal fees are paid in a timely manner and subject to any supplementary patent term that may be available).

5.1.3 THE PATENT FAMILY RELATING TO THE ISOLATION AND PURIFICATION OF SULFORAPHANE

This patent application relates to methods of isolating and purifying sulforaphane and more specifically to isolating and purifying sulforaphane from natural sources. The application also relates to methods of forming high purity complexes of sulforaphane with cyclodextrin.

The application was filed in respect of technology covered by the pipeline arrangements specified in the PharmAgra Agreement.

5.1.3.1 Summary of Patent Procedure to date

Priority date: 1 June 2012

International filing dates: 31 May 2013

Country	Application No.	Grant No.	Status
China	2013800402677	N/A	PENDING – awaiting first Office Action
Europe	EP13730628.8	N/A	PENDING – awaiting first Office Action
Japan	2015-514595	N/A	PENDING – awaiting first Office Action
USA	US14/404,781	N/A	PENDING – awaiting first Office Action

Inventors: Sahedeva Reddy Damireddi
Kpakpo Ambroise Akue
Jared K Nelson
Albert Robert Frisbee
Peter Wyatt Newsome

Owner: PharmAgra Labs Inc.

International Patent Application Number PCT/GB2013/051457 claimed priority from US 61/654,300 and was published on 5 December 2013 as WO 2013/179056. National phase applications were filed in China, Europe, Japan and the United States of America when the international procedure terminated.

WO 2013/179056 published with the following main claims:

1. A method of isolating sulforaphane and/or a sulforaphane analog from a natural source thereof, the method comprising:
    a) mixing the natural source of sulforaphane and/or sulforaphane analog with cyclodextrin in a suitable solvent and with or without heat;
    b) cooling the mixture to a temperature within the range of -10°C to +25°C to promote the formation of a precipitate of a complex between the sulforaphane or suloforaphane analog and the cyclodextrin; and
    c) collecting the precipitate formed.

11. A method of forming a complex of sulforaphane and/or a sulforaphane analog and cyclodextrin from a natural source of the sulforaphane and/or a sulforaphane analog, the method comprising:
    a) mixing the natural source of sulforaphane with cyclodextrin in a suitable solvent, and with or without heat;
    b) cooling the mixture to a temperature within the range of -10°C to +25°C to promote the formation of a precipitate of a complex between the sulforaphane and the cyclodextrin; and
    c) collecting the precipitate formed.

21. A complex of sulforaphane and/or a sulforaphane analog with cyclodextrin obtained by a process as defined in any one of claims 11 to 20.

22. A pharmaceutical composition comprising a complex of sulforaphane and/or sulforaphane analog with cyclodextrin according to claim 21 and one or more additional pharmaceutical excipients.

We understand that Evgen's core interest is in the chemical synthesis of sSFN. The purpose of this patent application is to provide a defensive position just in case any competitor tried to form sSFN directly from a natural source.

An International Search Report was issued by the European Patent Office (in its capacity as the International Searching Authority) on 19 August 2013. The International Search Report cited four prior art documents, namely:

1. Wu *et al.* Carbohydrate Polymers, 2010, Vol. 82, No. 3, 613 – 617;
2. WO 2008/091608;
3. CN 102688219; and
4. CN 102423492

The International Search Report indicates that document 1 is relevant to claims 1 to 22 presently on file and documents 2, 3 and 4 are relevant to claims 21 and 22 presently on file.

It is not unusual for prior art issues to be raised at this stage of the patent procedure. During the international phase, and in accordance with the normal patent prosecution procedure, no formal response to the International Search Report & Written Opinion was filed. HGF will work with PharmAgra and Evgen to address the issues raised during the prosecution of the national/regional phase patent applications derived from International Patent Application Number PCT/GB2013/051457.

5.1.3.2 Summary of the Rights conferred by this Patent Family

As indicated in Section 5.1.3.1 above, patent applications are currently pending in China, Europe, Japan and the United States of America.

Any granted patents obtained in these territories may be asserted against third party activity up until 31 May 2033 (provided renewal fees are paid in a timely manner and subject to any patent term extension or supplementary patent term that may be available).

Protection in the USA

The PCT claims outlined in Section 5.1.3.1 above are currently pending in the United States and the issuance of the first Office Action is awaited.

Protection in Europe

Following entry into the European regional phase, the European Patent Office issues an official communication (known as a Rule 161 and 162 EPC communication) inviting the applicant to: (i) make any desired voluntary amendments to the claims; (ii) pay any excess claims fees that are due; and (iii) comment on the objections raised in the International Written Opinion referred to above.

In response to this communication, the original PCT claims outlined in Section 5.1.3.1 above were amended to cancel claims 21 and 22 and the remaining claims were re-ordered in order to reduce the total number of claims and thereby reduce the number of excess claims fees that need to be paid. The cancellation of claims 21 and 22 was in response to objections raised by the Examiner during the international phase and the claims are now focused on the methodology of forming the complexes, which is the main focus of this invention. A divisional application could be filed at a later date in order to continue to pursue patent protection for the subject matter of claims 21 and 22 should Evgen wish to do so.

In response to the objections raised during the international phase (in the International Written Opinion), HGF provided some preliminary arguments in favour of the patentability of the remaining process claims in view of cited prior art relied upon by the Examiner. In due course, the European Examiner will consider the claim amendments made and the preliminary arguments presented as part of the substantive examination of this application. HGF will work with PharmAgra and Evgen to deal with any further objections that might be raised by the European Examiner.

Protection in other Jurisdictions

The claims pending in China and Japan correspond to the claims of the published international PCT application discussed in Section 5.1.3.1 above. HGF will work with PharmAgra and Evgen to deal with any objections raised when the examination of these applications commences.

5.1.4 THE PATENT FAMILY RELATING TO METHODS OF SYNTHESISING SULFORAPHANE

This patent application relates to methods of synthesising sulforaphane by reacting a compound of formula A (see below) with an oxidizing agent in an aqueous solvent and in the presence of a catalyst. The application also relates to methods of forming complexes of sulforaphane with cyclodextrin produced by the claimed methodology.

The application was filed in respect of technology covered by the pipeline arrangements specified in the PharmAgra Agreement.

5.1.4.1 Summary of Patent Procedure to date

Priority date: 1 June 2012

International filing dates: 31 May 2013

Country	Application No.	Grant No.	Status
Australia	201326930	N/A	PENDING – awaiting first Office Action
Brazil	1120140298416	N/A	PENDING – awaiting first Office Action
Canada	2875063	N/A	PENDING – awaiting first Office Action
China	2013800402624	N/A	PENDING – awaiting first Office Action
Europe	EP13726846.2	N/A	PENDING – awaiting first Office Action
India	10764/DELNP/2014	N/A	PENDING – awaiting first Office Action
Japan	2015-514596	N/A	PENDING – awaiting first Office Action
USA	US14/404,773	N/A	PENDING – awaiting first Office Action

Inventors: Sahedeva Reddy Damireddi
Kpakpo Ambroise Akue
Jared K Nelson
Albert Robert Frisbee
Peter Wyatt Newsome

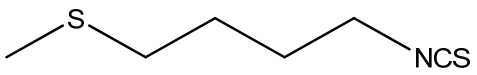
Owner: PharmAgra Labs Inc.

International Patent Application Number PCT/GB2013/051458 claimed priority from US 61/654,277 and was published on 5 December 2013 as WO 2013/179057. National phase applications were filed in Australia, Brazil, Canada, China, Europe, India, Japan and the United States of America when the international procedure terminated.

WO 2013/179057 published with the following main claims:

1. A process for the preparation of a complex of sulforaphane and cyclodextrin, the process comprising:

   (i) reacting, in an aqueous solvent, a compound of formula A:



A

   with an oxidizing agent and in the presence of a catalyst to form sulforaphane; and

   (ii) mixing the sulforaphane from step (i) with cyclodextrin in an aqueous solvent to form a precipitate of the sulforaphane-cyclodextrin complex.

16. A sulforaphane-cyclodextrin complex obtainable by a process as defined in any one of claims 1 to 15.

17. A sulforaphane-cyclodextrin complex according to claim 16 for use in the treatment and/or prevention of microbial infections and/or cancer.

18. A method of treating and/or preventing microbial infections and/or cancer, the method comprising administering to an individual in need of such treatment a therapeutically effective amount of a sulforaphane-cyclodextrin complex according to claim 16.

19. A pharmaceutical composition comprising a sulforaphane-cyclodextrin complex according to claim 16 and one or more additional pharmaceutical excipients.

The claims of this application cover a scaled-up process for synthesising sSFN that may be incorporated into a SULFORADEX® product.

An International Search Report & Written Opinion was issued by the European Patent Office (in its capacity as the International Searching Authority) on 19 August 2013. The International Search Report cited seven prior art documents, namely:

1. WO 2008/091608
2. Wu *et al.* Carbohydrate Polymers, 2010, Vol. 82, No. 3, 613-617
3. CN 102688219
4. CN 102423492
5. Holland *et al.*, Tetrahedron: Asymmetry, 1995, 6(7), 1569-1574
6. Schmid *et al.* Helvetica Chimica Acta, 1948, Vol. 31, No. 6, 1497-1505
7. Allessio *et al.* Journal of Agricultural and Food Chemistry, Vol. 56, No. 3, 875-883

The International Search Report indicates that claims 1 to 15 presently on file are considered to be novel in view of the cited prior art, but they are considered to lack an inventive step in view of a combination of documents 1 and 5 listed above.

It is not unusual for prior art issues to be raised at this stage of the patent procedure. During the international phase, and in accordance with the normal patent prosecution procedure, no formal response to the International Search Report & Written Opinion was filed. HGF will work with PharmAgra and Evgen to address the issues raised during the prosecution of the national/regional phase patent applications derived from International Patent Application Number PCT/GB2013/051458.

5.1.4.2 Summary of the Rights conferred by this Patent Family

As indicated in Section 5.1.4.1 above, patent applications are currently pending in Australia, Brazil, Canada, China, Europe, India, Japan and the USA.

Any granted patents obtained in these territories may be asserted against third party activity up until 31 May 2033 (provided renewal fees are paid in a timely manner and subject to any patent term extension or supplementary patent term that may be available).

Protection in the USA

The PCT claims outlined above in Section 5.1.4.1 are currently pending in the United States and the issuance of the first Office Action is awaited.

Protection in Europe

Following entry into the European regional phase, the European Patent Office issues an official communication (known as a Rule 161 and 162 EPC communication) inviting the applicant to: (i) make any desired voluntary amendments to the claims; (ii) pay any excess claims fees that are due; and (iii) comment on the objections raised in the International Written Opinion referred to above.

In response to this communication, and in order to address a number of the objections raised during the international PCT phase, the original PCT claims outlined in Section 5.1.4.1 above were amended to cancel claims 16, 17, 18 and 19. These amendments focus the claimed subject matter on scale-up process, which is the core of this invention. A divisional application could be filed at a later date in order to continue to pursue patent protection for the subject matter of claims 16, 17, 18 and 19 should Evgen wish to do so.

With regard to the remaining process claims (claims 1 to 15), HGF provided arguments to rebut the objection raised in the International Written Opinion that the subject matter of these claims was obvious in view of a combination of documents 1 and 5 of the International Search Report (listed in Section 5.1.4.1 above). In due course, the European Examiner will consider the claim amendments made and the preliminary arguments presented as part of the substantive examination of this application. HGF will work with PharmAgra and Evgen to deal with any further objections that might be raised by the European Examiner.

Protection in other Jurisdictions

The claims pending in Australia, Brazil, Canada, China, India and Japan correspond to the claims of the published international PCT application discussed in Section 5.1.4.1 above. HGF will work with PharmAgra and Evgen to deal with any objections raised when the examination of these applications commences.

5.2 IP COVERED BY A LICENCE OPTION AGREEMENT WITH CONSEJO SUPERIOR DE INVESTIGACIONES CIENTIFICAS (CSIC) AND UNIVERSIDAD DE SEVILLA

5.2.1 Terms of the Agreement

Evgen have entered into a Licence Option Agreement with Consejo Superior de Investigaciones Cientificas (CSIC) and Universidad de Sevilla in connection with sulforaphane analogues which are defined in an International application published as WO 2013/132124.

Under the terms of the agreement Evgen currently has an exclusive right to evaluate the efficacy of the analogues and, should the analogues be of interest to Evgen, has the exclusive right to negotiate a commercial licence.

5.2.2 THE PATENT FAMILY COVERING ANALOGUES OF SULFORAPHANE

This patent family concerns a series of sulforaphane derivatives and the optical isomer or enantiomer forms thereof; methods of making such derivatives; and the medical, food, cosmetic and dietary uses of said derivatives. The patent specification contemplates the use of the compounds alone or, alternatively, encapsulated in cyclodextrins.

HGF are handling the prosecution of this patent family under Evgen's instructions.

5.2.2.1 Summary of Patent Procedure to date

Priority date: 9 March 2012

International filing dates: 6 March 2013

Country	Application No.	Grant No.	Status
Australia	AU2013229355	N/A	PENDING – awaiting first Office Action
Canada	2,866,740	N/A	PENDING – awaiting first Office Action
China	201380013103	N/A	PENDING – awaiting first Office Action
Europe	EP13757087.5	N/A	PENDING – awaiting first Office Action
Japan	2014-560416	N/A	PENDING – awaiting first Office Action
USA	14/383,780	N/A	PENDING – awaiting first Office Action
Spain	P201230356	ES 2 425 294 B	GRANTED

Inventors: Noureddine Khiar el Wahabi
Immaculada y Fernandez Fernandez
Rocio Recio Jimenez

Owner: Consejo Superior de Investigaciones Cientificas (CSIC) and Universidad de Sevilla

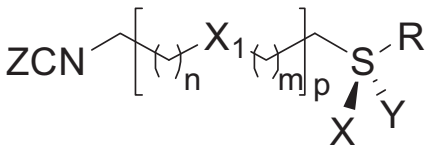
International Patent Application Number PCT/ES2013/070134 claimed priority from Spanish Patent Application No. P201230356 and was published on 12 September 2013 as WO 2013/132124.

National phase applications were filed in major jurisdictions when the international procedure terminated in September 2014. However these jurisdictions are not disclosed in this Report. This is because, at the time of writing, it is not possible for the public to identify at least some of these national patent applications and it is therefore considered commercially expedient to refrain from identifying them in a Report that will enter the public domain.

ES 2 425 294 B is the grant number for the Spanish priority application which was maintained in parallel to the international application.

WO 2013/132124 published with the following main claims:

1. A compound of general formula (I):



Formula (I)

where:

R is a linear, branched, cyclic, heterocyclic, aromatic cyclic, aromatic heterocyclic, saturated, or unsaturated chain or an NR^1R^2, where R^1 and R^2 are selected independently from the group consisting of H, linear, branched, cyclic, heterocyclic, aromatic cyclic, aromatic heterocyclic, saturated and unsaturated chain;

X and Y are selected from an oxygen atom and an electron pair, in such a way that if X is an oxygen atom then Y is an electron pair, or vice versa;

X1 is selected from the group comprising oxygen, sulphur, NR^3 and $^+NR^4R^5$, where R^3, R^4 and R^5 are selected independently from the group consisting of H, linear, branched, cyclic, saturated and unsaturated chain;

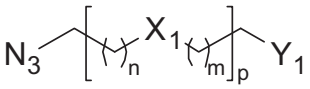
n and m denote a natural integer greater than or equal to 0;

p is a natural integer greater than or equal to 1; and

Z is sulphur or selenium.

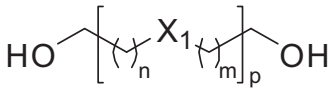
10. A method of obtaining a compound of formula (I) as described in any of the preceding claims, characterised in that it comprises the following steps:

(1) obtaining a compound of structure (V):



Formula (V)

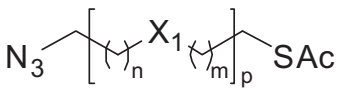
starting from a compound of formula (II):



Formula (II)

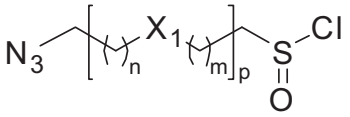
by transformation of the hydroxyls into good leaving groups, Y1, where Y1 represents a halogen atom or a sulphonate group; and a reaction of nucleophilic substitution of one of these leaving groups, Y1, with sodium azide in an organic solvent, resulting in incorporation of the azide function in the compound of formula (V);

(2) reacting the compound of formula (V) obtained in the preceding step with potassium thioacetate, in an organic solvent, to give the compound of general formula (VI):



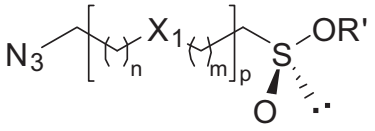
Formula (VI)

(3) reacting the compound obtained in step (2) with sulphuryl chloride and with acetic anhydride, in an organic solvent, at low temperature to give the sulphinyl chloride of structure VII:

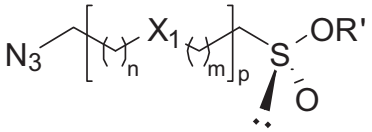


Formula (VII)

(4) reacting the compound obtained in step (3) with a chiral secondary alcohol derived from carbohydrates R'OH, in an organic solvent at low temperature and in the presence of a sterically hindered base or of a base that is not sterically hindered, to produce a compound of structure (VIII) or of structure (VIIIa), respectively:

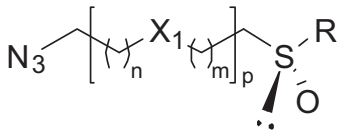


Formula VIII

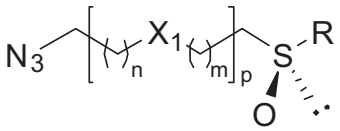


Formula VIIIa

(5) reacting the compound (VIII) or compound (VIIIa), obtained in the preceding step (4), with a compound selected from the group consisting of an organometallic compound of formula R^6M, a Grignard reagent R^6MgX^2, and an R^1R^2NM, where R^6 is selected from the group consisting of linear, branched, cyclic, heterocyclic, aromatic cyclic, aromatic heterocyclic, saturated and unsaturated chain; R^1 and R^2 have the same meaning as defined for general formula (I); X^2 is a halogen atom and M is a metal atom in an organic solvent at low temperature to obtain a product of formula (IX) or formula (IXa), respectively:



Formula (IX)

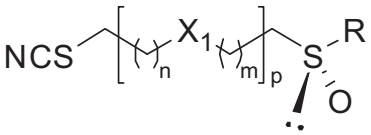


Formula (IXa)

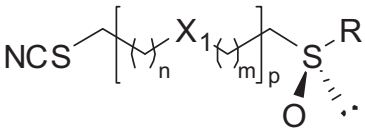
and

(6) transforming the azide group of the compound of formula (IX) or (IXa) from the preceding step into a group ZCN, in such a way that:

(6') in the case when Z is sulphur in general formula (I), said transformation comprises reacting the compound IX or the compound IXa obtained in step (5) with a triarylphosphine in an organic solvent, heating, and in a second step with carbon disulphide, to obtain the product of formula (X) or (Xa), respectively:



Formula (X)

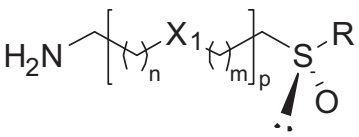


Formula (Xa)

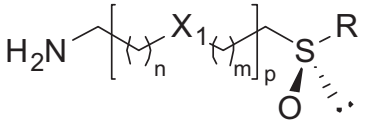
or

(6'') in the case when Z is selenium in general formula I, said transformation comprises

(6''a) reacting the azide of compound (IX) or (IXa) with a reducing agent, to obtain a product of formula (XI) or formula (XIa) respectively:

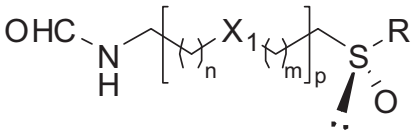


Formula (XI)

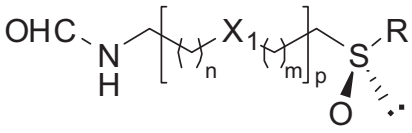


Formula (XIa)

(6''b) reacting the compound obtained in step (6''a) of formula XI or XIa, with a formyl-group transfer agent, to give the compound of formula XII or XIIa respectively:



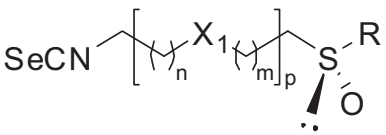
Formula (XII)



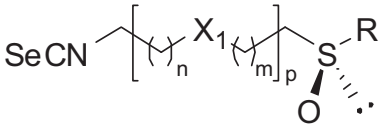
Formula (XIIa)

and

(6''c) transforming the formamide obtained in step (6''b) of formula XII or XIIa, into an isoselenocyanate of formula XIII or XIIIa, with thiophosgene and selenium, in the presence of a base and in an organic solvent:



Formula (XIII)



Formula (XIIIa)

where n, m, p, X1 and R are defined as in claim 1.

21. A composition that comprises in its formulation at least one compound as described in any one of claims 1 to 9.

22. Composition according to the preceding claim, where the compound is encapsulated in a cyclodextrin.

24. Composition according to the preceding claim, wherein the pharmaceutical composition further comprises at least one additive or pharmaceutically acceptable vehicle.

26. Compound according to any one of claims 1 to 9, or of the composition described in any one of claims 21 to 25 for use in medicine.

29. Compound or composition according to any one of claims 26 to 28, for preventing and treating cancer, selected from the group comprising cancer of the breast, skin, gastrointestinal tract, respiratory tract, colon, stomach, oesophagus, lung, oral cavity, pharynx, endometrium and pancreas; and preferably for pancreatic, colon and/or gastric cancer caused by the action of *Helicobacter pylori*.

Evgen is evaluating the sulforaphane derivatives defined by these claims under the terms of the option agreement and on the basis that such derivatives (claim 1); methods of making them (claim 10), encapsulation of such derivatives with cyclodextrin (claim 22); and their medical use (claim 26) in a number of conditions which include cancer (claim 29) may represent technology that is complementary to the Company's interest in SULFORADEX® (i.e. sulforaphane complexed with cyclodextrin).

5.2.2.2 Summary of the Rights conferred by this Patent Family

Applications derived from PCT/ES2013/070134

Filing formalities were completed relatively recently for national phase applications derived from PCT/ES2013/070134. Accordingly no substantive office actions have issued from the respective patent offices and it is not possible to confirm when, or even if, each of these applications will proceed to grant.

Nevertheless a laudatory IPRP (produced by the Spanish Patent Office) issued for PCT/ES2013/070134 and states that the International Authorities believed that the documents cited in the ISA were considered to not be relevant against the claims published with WO 2013/132124. Each of the cited documents were considered to only represent technological background and were not thought to be relevant against patentability. HGF have not reviewed the relevance of these documents for the purposes of this report and at least the USPTO will conduct further searches and/or come to their own conclusions of the relevance of the cited documents. However this favourable report is very likely to result in many of the patent offices being willing to grant patents, on the basis of the claims published with WO 2013/132124. We therefore believe that the applicants, and Evgen, can be optimistic that prosecution will proceed without significant objections from Patent Examiners and early grants would seem likely.

Protection in the USA

The PCT claims outlined above in Section 5.2.2.1 are currently pending in the United States and the issuance of the first Office Action is awaited.

Protection in Europe

Following entry into the European regional phase, the European Patent Office issues an official communication (known as a Rule 161 and 162 EPC communication) inviting the applicant to: (i) make any desired voluntary amendments to the claims; (ii) pay any excess claims fees that are due; and (iii) comment on any objections raised in the International Written Opinion. Given that the International comments were laudatory, it was not necessary to comment on any objections and only minor amendments were made to the PCT claims which did not limit the scope of the claims. These amendments were made to reduce the excess claims fees that were payable.

HGF awaits a first substantive Examination Report from the European Patent Office and is optimistic that the Examiner will not raise any major objections to the pending claims.

Spanish Rights

ES 2 425 294 B proceeded to grant with claims identical to those filed with PCT/ES2013/070134, but without undergoing substantive examination by the Spanish Patent Office (as permitted in Spain). Under normal circumstances a patent granted under such a procedure would not be assumed to define valid claims and an assessment would be required. However the favourable IPRP for PCT/ES2013/070134 does significantly strengthen the value of this patent because the Spanish authorities (acting as the ISR) failed to locate any documents that they considered to be relevant against the claims as granted and it would have been very unlikely that a substantive examination in Spain would have objected to any of the claims.

Granted patents derived from PCT/ES2013/070134 may be asserted against third parties until 6 March 2033 (provided renewal fees are paid in a timely manner and subject to any patent term adjustments or extensions that may be available). ES 2 425 294 B may be asserted against third parties until 9 March 2032 (provided renewal fees are paid in a timely manner and subject to any patent term extension that may be available).

5.3 UNPUBLISHED IP AND KNOW HOW

Evgen is regularly generating technical information which is kept company secret until a decision is made with regards establishing a patent position.

It is clearly a commercial imperative that such information is kept confidential. Therefore three areas that may give rise to future IP are only briefly outlined below:-

5.3.1 INVENTION PROPOSALS THAT MAY BE DERIVED FROM RESEARCH CONDUCTED UNDER MTAs

Evgen have advanced preclinical research by providing a number of institutions with sSFNs under the terms of Material Transfer Agreements (MTAs).

Details of these agreements will not be discussed in any detail for the sake of commercial confidentiality. However we have noted that recipients of sSFNs are generally required to disclose any putative inventions to Evgen and Evgen may then make arrangements to file patent applications to protect any such inventions. The MTAs include provisions for Evgen to exercise an option to an exclusive royalty bearing licence(s) under any such patents filed in the name of the recipient institution.

We understand that Evgen carefully reviews the reports from work conducted under the MTAs and, if appropriate, generate an Invention Disclosure Record and seek the opinion of a patent attorney with regards a patentable angle.

We have reviewed a first Invention Disclosure Record that concerns a potential new use for sSFN that has come to light from research conducted under one of these MTAs. The proposal appears to be patentable in principle and we understand that Evgen is considering its options for establishing a priority date for a new patent family.

5.3.2 INVENTION PROPOSALS DERIVED FROM CONTRACT RESEARCH OR CONTRACT MANUFACTURING

Evgen have used, or intends to use, Contract Research Organisations (CROs) and manufacturers to prepare drug products for further investigational work and to conduct work that may be used to generate data that will be required in the preparation of dossiers that will need to be submitted to regulatory authorities as development progresses.

We are satisfied that the Company's management understand that any agreements covering this sort of development work should include clauses that explicitly assign IP rights.

We are also satisfied that the Company's management understand that it is important to identify (and document in an Invention Disclosure Form) whether an inventive contribution is made by (a) employees or officers of Evgen; (b) staff at the contract organisation; or (c) a combination of the two. This is important for establishing a chain of title for any IP that derives from work carried out under contract (or otherwise).

We have reviewed a second Invention Disclosure Record that relates to certain drug product formulations comprising sSFNs that are manufactured by contractors. Again the technology appears to be patentable in principle and we understand that Evgen is considering its options for establishing a priority date for a further new patent family. The Record identifies an Officer of Evgen as the sole inventor and Evgen believes that any work carried out under contract was, or will be, technical in nature rather than inventive. Accordingly this appears to be an opportunity for the Company to establish a patent filing in its own and sole name.

5.3.3 INVENTIONS CONCEIVED AND KNOW-HOW CURRENTLY RETAINED WITHIN EVGEN

We have reviewed a third Invention Disclosure Record which concerns dosing regimens for drug products comprising sSFNs. Dosing regimens are patentable in principle and we recommend that the Company establishes a patent position for any dosing regimens that will be covered by a market authorization. We understand that the Company is considering its options for a further new patent family. The Invention Disclosure Record we have reviewed also identifies Officers of Evgen as the sole inventors. Accordingly this appears to be a further opportunity for the Company to establish a patent filing in its own name.

5.4 THE COMPANY'S TRADE MARK PORTFOLIO

Patent coverage of the technology being developed is clearly the Company's highest priority insofar as IP protection is concerned. However HGF have briefly reviewed Evgen's trademark portfolio and provide our comments in this section.

5.4.1 SULFORADEX®

Country	Trade Mark No.	Filed	Registered
United Kingdom	2538957	12 February 2010	21 May 2010
European Union (CTM)	010289528	26 September 2011	30 January 2012
USA	85432458	26 September 2011	7 August 2012

Proprietor: Evgen Limited

5.4.1.1 European Rights

Rights have been registered for the European Union and a separate mark also exists on the UK register.

Registration of the use of the SULFORADEX mark has been secured in connection with:

> Pharmaceutical preparations; pharmaceutical products; and pharmaceutical preparations and products for use in the treatment of cancer (in International class 5).

5.4.1.2 US Rights

During prosecution the US Examiner objecting to SULFORADEX as a trade mark in the US because he considered it to be confusingly similar to the mark SULFOXYDEX (for medicated shampoos in veterinary use).

The objection was overcome by restricting the goods and services covered by the US mark to:

> Pharmaceutical preparations and products for human use in the prevention and treatment of cancer; pharmaceutical preparations and products for human use in the prevention and treatment of inflammatory diseases, disorders and conditions (in International class 5).

5.4.1.3 Summary

Trademark registration in the UK. European Union and the US would seem appropriate coverage for the SULFORADEX brand at this stage in development.

We are not sure to what extent clearance searches were conducted before the SULFORADEX mark was adopted. Evgen should review this before too much is invested in the brand. This is because it is possible that prior rights (in addition to the SULFOXYDEX issue) may exist in some jurisdictions that could make it difficult to use your chosen mark.

In addition to the issues relating to clearance searching it should be borne in mind that regulatory authorities (and particularly the FDA) can decide (independent of any trade mark law or practice) that a brand name is unacceptable because there is a risk it would be mistaken for a different drug that is marketed for other purposes.

It should be noted that the adoption of the SULFORADEX® mark is a matter of branding and we do not believe it would represent a significant issue for Evgen if, in the worst case scenario, a completely new brand would need to be adopted in the future.

5.4.2 EVGEN®

Country	Trade Mark No.	Filed	Registered
United Kingdom	2496447	1st September 2008	26th December 2008

Proprietor: Evgen Limited

> EVGEN has been registered in the UK in respect of the following goods and services:
>
> Class 5:
>
> Pharmaceutical preparations; pharmaceutical products; food supplements for nutritional purposes; food supplements for dietary purposes; food supplements for medicinal purposes; preparations for use as additives to foods for human consumption; preparations for use as additives to drinks for human consumption; health food supplements; health care products.
>
> Class 36:
>
> Financial services; services for the funding of venture capital; services for the provision of venture capital; investment research services; information and advisory and consultancy services relating to all of the foregoing.

Class 42:

Scientific research services; scientific evidence assessment services; product assessment services; product development services; conducting of clinical trials; designing of brand names; information and advisory and consultancy services relating to all of the foregoing.

The house mark EVGEN has only been registered in the United Kingdom. However this appears appropriate at this stage in the development of the company because we understand that it is likely that more value will be attached to the branding of Evgen's lead product SFX-01 (which could ultimately be branded as SULFORADEX®) rather than the Company name *per se.*

The Company should consider expanding protection for the mark EVGEN in view of the increased international publicity that will be associated with a stock market listing.

6. THIRD PARTY PATENT RIGHTS OR INTERACTIONS OF RELEVANCE TO THE COMPANY

6.1 FREEDOM-TO-OPERATE (''FTO'')

The Company needs to maintain its rights in connection with the PharmAgra patent families discussed in Section 5 above for it to be free to commercialise SULFORADEX®.

A general freedom-to-operate can only be established if a business has conducted a detailed enough review of third parties rights that may limit its commercial aims. As outlined below, and in view of the current stage of product development, we believe that Evgen has conducted adequate due diligence in connection with investigating such third party patent rights.

6.1.1 Patent landscaping/state-of-the art exercise conducted in April 2012

Bioscience IP conducted a patent landscaping/state-of-the art exercise in April 2012 with a remit that included forming a preliminary view on whether or not any third party patent rights exist that may impede the commercialisation of sSFN.

It was felt that there would be limited value in searching for patents that protected sulforaphane alone or pharmaceutical compositions defined by the fact that they comprise sulforaphane. This was because:

(a) Sulforaphane's potential as an anticancer drug was first reported by Zhang *et al.* at The John Hopkins University School of Medicine in March 1992 (Proc Natl Acad Sci (1992) Vol. 89 pp2399-2403); and

(b) Patents generally have a life-span of 20 years and it therefore stands to reason, in view of at least Zhang *et al* (1992)., that any ''platform'' patents covering sulforaphane as a drug *per se*, and as an anticancer drug in particular, will have expired or soon will expire. Furthermore the timetable envisaged for the commercial launch of a SULFORADEX® product means that there should be negligible risk of any valid patent generically covering pharmaceutical compositions that are characterised by the fact that they comprise sulforaphane.

For similar reasons it was also felt that there would be limited value in searching for patents that protected cyclodextrin as a pharmaceutical carrier because such a use has been known for well over 20 years. Accordingly there should not be any platform patents relating to α-cyclodextrins *per se* that could impede the Company.

The 2012 exercise therefore focused on cyclodextrin-sulforaphane complexes. There were no limitations with regards (i) the intended use; or (ii) the final formulation of a SULFORADEX® product (both of which were then, and to a lesser extent still, being resolved).

52 patent families were considered during the 2012 exercise and none of them were reported to represent major obstacles to developing α-cyclodextrin-sulforaphane complexes as a drug product for the prevention or treatment of most cancers. Seven patent families were identified as being of interest to Evgen but were not considered to be relevant against the use of a SULFORADEX® product in the treatment of prostate cancer.

HGF has reviewed the status of the seven families identified by Bioscience IP and have noted that, since 2012, a number of the cases have expired; will expire before any product may be marketed; or have been abandoned. It is our view that none of the seven patent families will impinge on the commercial development of SULFORADEX® products for treating prostate cancer, breast cancer or subarachnoid haemorrhage.

6.1.2 Patent landscaping/state-of-the art exercise conducted in October 2014

As part of our review of Evgen's IP position, HGF commissioned a searching organisation to:

(i) Conduct a ''top-up'' search to extend the April 2012 searches to cover patent documents published up until the end of September 2014; and

(ii) Conduct supplementary state of the art searches specifically covering the use of sulforaphane-cyclodextrin complexes for treating prostate cancer, breast cancer or subarachnoid haemorrhage.

A further 36 patent families were highlighted by the searchers conducting the ''top-up'' search; 8 patent families were highlighted by the searchers in connection with the treatment of subarachnoid haemorrhage; and 20 patent families were highlighted by the searchers in connection with the treatment of breast or prostate cancer.

HGF have reviewed each of these patent families and we do not believe any of them will impinge on the commercial development of SULFORADEX® products for treating prostate cancer, breast cancer or subarachnoid haemorrhage.

6.1.3 Further Freedom-to-Operate Searching

In 2012 Bioscience IP expressed the view that it did not appear appropriate, at the time, for Evgen to conduct a full freedom to operate exercise. This was because product development was at a relatively early stage. The formulation of the commercial product and even a clinical use had not been decided. It was therefore impossible to make a formal infringement assessment and advise on freedom to operate because it was not possible at the time to define the commercial activity which may, or may not, fall within the scope of the claims of third party patents. It was suggested that product development may reach a stage sometime in 2014/2015 or thereafter when a more formal assessment may be possible.

HGF supports this view and is of the opinion that at the date of this report the exercises described in 6.1.1 and 6.1.2 above represent an appropriate level of third party IP due diligence in view of the current stage of the Company's development programmes.

The Company should at least finalise protocols for Phase II trials before commissioning a further freedom-to-operate exercise. This will only be possible when full details are known regarding: (a) the specific formulation, and dosing regimen, of a SULFORADEX® product; (b) the specific processes employed to make the commercial product; and (c) the specific treatment that is likely to be covered by a marketing authorisation. We understand that the Company will have addressed these issues sometime during 2016.

FTO assessments should always be expanded and refined as products approach the market. HGF also believe it would be prudent, and probably only possible, to conduct a definitive FTO exercise after Phase II trial(s) have reported, but such an exercise should be considered before a market authorisation is sought and preferably before investing in Phase III clinical trials for a SULFORADEX® product.

6.2 THIRD PARTY ACTIONS OR INTERACTIONS

We are not aware of any potential or pending IP-related litigation or patent office opposition proceedings involving Evgen or the Company.

We are also not aware of any specific third party rights, other than those mentioned above (e.g. the PharmAgra cases which are in any event licensed to Evgen), that may be used to limit the Company's commercial aims for its key development areas. We have outlined in this Report when we believe it would be prudent to conduct more sophisticated freedom-to-operate searches.

Furthermore are we not aware of any third party actively developing commercial products that fall within the scope of Evgen's patent portfolio or licensed IP. However the patent landscaping/state-of-the art exercises outlined at 6.1.1 and 6.1.2 above have identified a number of patent applicants who may well require a licence from Evgen before they would be free to commercialize sSFN as contemplated in their own patent specifications.

Yours faithfully

PAUL BANFORD
For HGF Limited

PART V

TECHNOLOGY EXPERTS' REPORT

Set out below is the text of a report on the Group by PharmaVentures Limited, the technology experts.

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Dear Sirs,

Evgen Pharma plc (''Evgen Pharma'' or the ''Company'')

PharmaVentures Limited (''PharmaVentures'' is an independent pharmaceutical business consultancy that specialises in assisting biomedical company clients in forming alliances or conducting M&A and also performs technical and commercial evaluations of pharmaceutical and biotechnology products, product portfolios and companies. PharmaVentures has built up considerable expertise in the analysis of healthcare markets, biopharmaceutical companies and their technologies.

PharmaVentures has been instructed by the Directors of Evgen Pharma plc and Northland Capital Partners Limited to prepare an independent report on the Company for inclusion in its admission document dated 15 October 2015 covering a technical and commercial assessment of the Company's lead compound SFX-01 and an overview of the markets targeted by Evgen Pharma (and its wholly-owned subsidiary, Evgen Limited (''Evgen'')) including competitive products in the market and in development. SFX-01 was generated by the Company's proprietary Sulforadex® technology. Our report is being prepared pursuant to Rule AR 4 of Schedule 3 of the AIM Rules for Nominated Advisers issued by the London Stock Exchange in order to provide technical comfort to the Members of the Evgen Pharma Board of Directors and to Northland Capital Partners Limited.

In preparing this report, PharmaVentures interviewed members of the Evgen management team and reviewed relevant Company documentation and scientific literature. These sources were supplemented by PharmaVentures' extensive internal and external resources, experience and understanding of the global pharmaceutical industry.

It should be noted that PharmaVentures does not comment on the validity or enforceability of any patent applications taken by the Company. Patents may play a key role in the commercialisation plans of Evgen and the patent applications are fully discussed in the report of the patent attorneys, HGF Limited, set out in Part IV of this document.

This report has been prepared with due diligence based on the information provided by Evgen or taken from public domain sources deemed to be reliable by PharmaVentures. While every effort has been made to ensure the accuracy and completeness of the information and data presented, PharmaVentures cannot accept liability for errors or omissions. In particular, the industry areas under examination are fast moving and any change in circumstances may render some or all of the information or conclusions incomplete, obsolete or invalid.

PharmaVentures is a pharmaceutical industry consultancy and is not an investment advisor. This report is specifically limited to the matters set out above and is not to be taken as giving any advice on the merits of an investment in Evgen Pharma.

1. Summary

Evgen Pharma is a UK based clinical stage pharmaceutical company focussed on the development and commercialisation of sulforaphane-based pharmaceuticals for a number of indications, with patient trials planned in breast cancer and subarachnoid haemorrhage (“SAH”).

Sulforaphane is a well-established antioxidant inflammation modulator, which was first identified as an anti-cancer agent in 1992. The protective qualities of sulforaphane are mediated by activation of Nuclear factor (erythroid-derived 2)-like 2 (“Nrf2”), a key component in a major antioxidant pathway, and inhibition of a major pro-inflammatory cascade by inhibiting nuclear factor kappa-light-chain-enhancer of activated B cells (“NF-$_K$B”).

There is a substantial body of scientific literature that confirms the preclinical efficacy of sulforaphane preparations in over 30 animal models of different diseases, including breast cancer and prostate cancer. Despite the significant promise of sulforaphane, it has historically been difficult to develop drugs based on this chemical due to its highly reactive and unstable nature, which requires storing synthetic sulforaphane at -20°C in dessicating conditions.

This considerable disadvantage has been overcome by the stabilisation of sulforaphane in a scaffold of α-cyclodextrin, which has resulted in a powder that has proven to be stable at room temperature through to the last time point measured at two years. This pharmaceutical preparation is known as SFX-01 and is expected to be registered as a new chemical entity, which should give it significant commercial protection. Evgen licensed the exclusive worldwide rights to the Sulforadex® intellectual property from PharmAgra Labs Inc. and Lalilab Inc., with the exception of topical applications as referenced below.

SFX-01 has successfully completed animal safety and toxicology testing without any adverse effects up to an equivalent dose of 700mg per day in man. Evgen has since successfully completed two Phase I clinical studies in human subjects with SFX-01, which demonstrated that the drug has excellent tolerability and safety together with good bioavailability and pharmacokinetics, characteristics essential for successful drugs.

The proposed clinical development strategy for SFX-01 is focused on developing the drug for markets that currently have significant clinical needs or little or no competition.

Breast cancer is the most common cancer globally with nearly 1.7 million new cases diagnosed in 2012. The treatment of the disease depends on various factors such as the stage of the cancer and the type of receptors expressed on the surface of the cancer cells, and can involve surgery, radiotherapy and chemotherapy. Approximately two thirds of all breast cancers contain receptors to hormones such as estrogen and progesterone, and those breast cancers expressing estrogen receptors are treated with endocrine therapies that block the estrogen receptor pathway such as tamoxifen and aromatase inhibitors. Whilst blockade of this pathway is highly effective, intrinsic and acquired resistance to endocrine therapy is common.

One potential source of resistance is thought to come from a sub-population of breast cancer cells known as cancer stem cells (“CSC”). Evgen has demonstrated that SFX-01 can inhibit breast CSCs in a number of in vitro and in vivo models of breast cancer. Accordingly, Evgen is initially targeting refractory patients and plans to examine the potential synergies of adding SFX-01 to a commonly used second-line therapy such as fulvestrant (Faslodex) on the progression free survival of post-menopausal patients with ER+ metastatic breast cancer.

Evgen is also developing SFX-01 for the potential orphan drug indication of subarachnoid haemorrhage, seeking to reduce vasospasm-induced decline in cognitive function that occurs three to five days after the initial bleed. Only one drug is approved to treat this aspect of SAH, a calcium

channel blocker called nimodipine. SFX-01 is expected to be used as an adjunct to the well-established but all too infrequently effective nimodipine.

With sufficient resources Evgen believes that SFX-01 also has application in a number of other indications including prostate cancer, multiple sclerosis (''MS''), osteoarthritis (''OA'') and chronic obstructive pulmonary disease (''COPD'').

Assuming that the results of the planned clinical trials and subsequent development are successful, Evgen, or a partner, would be well-placed to attain approval to market SFX-01. A stronger clinical package will also allow Evgen to further its discussions with regard to the licensing of marketing rights to its product in the major pharmaceutical markets, and retain a greater proportion of the future value of its commercialisation.

2. Market Overview

Evgen intends to develop SFX-01 for a number of different diseases including cancers and neurological disease where the broad spectrum cytoprotective qualities of the sulforaphane active may be clinically useful.

2.1. Breast Cancer

Breast cancer is the most common invasive cancer in women in the developed and less developed world. In 2011, the WHO estimated 508,000 women died of the disease, which appears to be most prevalent in Western Europe. It is 100 times more common in women than men. The outcome for breast cancer depends on the type of cancer, extent of disease and person's age. In the developed world, survival rates are high with up to 80 to 90 per cent of patients surviving for at least five years post diagnosis.

Estimated Five Year Prevalence and Incidence of Breast Cancer

Country	Five Year Prevalence	Incidence
WW	6,255,000	1,677,000
US	971,000	233,000
EU28	1,467,000	367,000

Source: GloboCan, 2012

Breast cancers are classified according to several systems according to histopathological status, grade and stage of the tissue, as well as the receptor status of the breast cancer cells. Breast cancer cells have three important types of receptors: estrogen receptors, progesterone receptors and HER2 receptors.

Treatment of the disease depends on various factors, such as stage of the cancer. Breast cancer is usually treated with surgery followed by chemotherapy or radiotherapy. Patients who have no detectable cancer after surgery are often given adjuvant or neo-adjuvant therapy to prevent the return of the cancer. Often in the early stages of breast cancer, it is thought that some cancer cells break away from the primary breast tumour and begin to spread (metastasise). Some patients are treated after or at the same time as surgery (adjuvant), or before surgery begins (neo-adjuvant).

In addition to conventional chemotherapy, drug companies have developed a number of hormone, targeted and bone-directed therapies for the treatment of breast cancer. The cellular receptor status of the cancer determines the use of targeted pharmaceutical intervention.

About two out of three breast cancers are hormone receptor positive, containing receptors of hormones such as estrogen or progesterone. For example, cancers with estrogen receptor positive cells are treated with blockers of estrogen receptor pathway which include reducing the levels of estrogen (e.g. aromatase inhibitors), antagonising estrogen receptor function (e.g. tamoxifen and other selective estrogen receptor modulators) or down regulating estrogen receptor levels (e.g. Faslodex/fulvestrant). Despite good efficacy in many patients treated with endocrine therapy, approximately one third of women treated with tamoxifen and other endocrine therapies eventually acquire resistance to endocrine therapy and the disease recurs. A number of different mechanisms are implicated in the acquisition of resistance to endocrine therapy, including a role for cancer stem cells which generally do not express endocrine receptors.

Approximately 20 per cent of advanced breast cancers are positive for another protein marker called HER2 (human epidermal growth factor receptor 2). Tumours positive for HER2+ receptors are treated with targeted therapies such as Herceptin, Kadcyla, Perjeta and Tykerb. Certain breast cancers, referred to as triple negative cancer cells, are those that lack receptors for any of the three important types of breast cancer receptor. Other targeted therapies include drugs like Afinitor and Avastin.

The market for breast cancer is large, and is expected to reach US$15 billion by 2022 according to a recent report by Decision Resources (2013). Anti-estrogen agents have been around since the early 1970's and many of the drugs used to treat endocrine receptor positive cancers are now off-patent and much of the growth in the market is coming from increasing use of anti-HER2 therapies. However, historically, endocrine receptor-based treatments have been highly successful from a commercial and clinical perspective, with several blockbuster drugs such as the aromatase inhibitor Arimidex which peaked at $1.9 billion sales in 2009. Even today, sales of AstraZeneca's Faslodex are expected to approach $1 billion by 2020 despite being approved in the US for the treatment of hormone receptor positive metastatic breast cancer, whose disease has spread after treatment with anti-estrogen medicine.

Selected Marketed Breast Cancer Drugs

Company	Product	Generic Name	Pharmacological Class	WW Sales 2013 ($M)	WW Sales 2020 ($M)
Roche	Herceptin	trastuzumab	Anti-HER2 (ErbB-2) MAb	6,178	5,229
Roche	Perjeta	pertuzumab	Anti-HER2 (ErbB-2) MAb	1,004	3,587
Pfizer	Ibrance	palbociclib	Cyclin-dependent kinase (CDK) 4 & 6 inhibitor	—	3,400
Roche	Kadcyla	ado-trastuzumab emtansine	Anti-HER2 (ErbB-2) MAb-DM1 maytansinoid conjugate	517	1,288
AstraZeneca	Faslodex	fulvestrant	Oestrogen antagonist	720	814
Celgene	Abraxane	paclitaxel (albumin-bound)	Taxane	495	485
Eisai	Halaven	eribulin mesylate	Microtubule/tubulin inhibitor	323	441
Novartis	Afinitor	everolimus	Mammalian target of rapamycin (mTOR) inhibitor	235	385
Novartis	Tykerb	lapatinib ditosylate	EGFr & HER2 (ErbB-2) dual kinase inhibitor	—	240

Source: EvaluatePharma

2.2. Subarachnoid Haemorrhage

Subarachnoid haemorrhage is a neurological condition that is characterised by bleeding on the surface of the brain. This bleeding can result in increased pressure on the brain, blockage of regular cerebrospinal fluid ("CSF") circulation and vasospasm, leading to secondary stroke[1]. 85 per cent of SAH cases result from the rupture of an intracranial aneurysm[2], whilst 10 per cent are attributable to non-aneurysmal perimesencephalic haemorrhage, and the remaining 5 per cent result from various rarer causes, including lesions of cerebral and spinal vasculature and tumours[2]. SAH is estimated to account for 5 per cent of all strokes[3], and studies by the World Health Organisation indicate that depending on the country, the annual incidence of SAH ranges from 2 –

1 Mayfield Clinic, 2013, http://www.mayfieldclinic.com/PE-SAH.HTM#.VDewMvldXwY

2 Gijn, J. et al., 2007, *Subarachnoid haemorrhage*, **The Lancet**, 369: 306 – 369

3 King JT Jr. *Epidemiology of aneurysmal subarachnoid hemorrhage*. **Neuroimaging Clin N Am**. 1997; 7: 659-668

23 cases/100,000 population[4], with an aggregate worldwide incidence of 10.5 in 100,000 person-years[5].

Cerebral aneurysms commonly arise at sites of arterial branching, and are often found on the arteries of the Circle of Willis. While the risk of aneurysm rupture is small, SAH carries a high overall mortality rate of up to 67 per cent[6], and less than a third of patients are able to return to their previous occupation and lifestyle[7]. Given the age-related incidence and high morbidity and mortality, SAH places a high burden on society due to the loss of productivity and used resources[8].

SAH treatment is primarily directed towards prevention of further bleeding by isolation of the aneurysm from the cerebral circulation via coiling or clipping of the aneurysm sac. However, these measures do not address the morbidity and mortality associated with delayed onset ischaemia (DCI). While the mechanisms underlying DCI are not yet understood, they are commonly initiated by extracellular haemoglobin released as red blood cells in the subsequent clot are lysed, which results in direct neurotoxicity, increased oxidative stress and further injury[9].

Currently, the most commonly utilised therapeutic for the reduction of DCI risk is nimodipine, a calcium channel blocker[10], which has been shown to reduce arterial constriction and to improve cerebral blood flow. However, the mechanism of action of nimodipine in SAH is not yet understood, and it is believed to have little effect on reducing delayed vasospasm, with poor outcomes remaining a significant problem as evidenced by contemporary outcome data since its introduction[11]. Moreover, even in the case of survivors conventionally considered to have made a good recovery, neurocognitive deficits are common, leading to extensive problems with social reintegration and functioning in the workplace[12].

We estimate that the total addressable SAH population would be approximately 120,000[13] which may qualify SFX-01 for orphan drug status in commercially important jurisdictions such as the US and Europe. The categorisation of SAH as an orphan disease has certain economic and regulatory advantages for drug developers, such as making it easier to gain marketing approval and extended periods of market exclusivity for specific treatments. Given the lack of efficacy of existing treatments for SAH, a clinically effective agent with patent life or market exclusivity could yield meaningful and early revenue for the developers of SFX-01.

2.3. Multiple Sclerosis

Multiple sclerosis is an inflammatory disease of the central nervous system where the insulating tissue around nerve cells in the brain and spinal cord is damaged. This damage can result in disruption of the ability of the nervous system to communicate, manifesting itself in physical, mental and sometimes psychiatric problems. There are several forms of multiple sclerosis; relapsing forms where the symptoms occur in isolated attacks with a degree of recovery, and progressive forms where symptoms build up over time. The worldwide prevalence of the disease is estimated by the WHO at between 2.0 and 2.5 million, with a higher rate of incidence in certain populations of Northern European descent. Diagnosis is usually made in the late twenties and early thirties.

Treatments for multiple sclerosis attempt to improve function after an attack or prevent new attacks. For many years, the mainstay of treatment for relapsing forms of MS was based on immune modulating interferons and Copaxone. Despite relatively limited efficacy and some prominent adverse events, these drugs have been commercially successful. According to Datamonitor, the market for multiple sclerosis drugs is currently valued at $12 billion and its growth is expected to be driven by the emergence of a group of novel oral therapies: Gilenya, Aubagio

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4 Bederson et al., 2009, *Guidelines for the Management of Aneurysmal Subarachnoid Hemorrhage*, **Stroke**

5 Suarez, J. I., 2007, *Non-traumatic Subarachnoid Hemorrhage*, **Intensive Care Medicine**, pp. 721-731

6 Nieuwkamp, Dennis J., et al., 2009, Changes in case fatality of aneurysmal subarachnoid haemorrhage over time, according to age, sex, and region: a meta-analysis, **The Lancet Neurology**, 8.7: 635-642.

7 Ferro et al, 2008, Update on subarachnoid haemorrhage: Review, **Journal of Neurology**, 255: 465-479

8 Kreiter, Kurt T., et al., 2002, Predictors of cognitive dysfunction after subarachnoid haemorrhage, **Stroke** 33.1: 200-209.

9 Pluta, Ryszard M., et al., 2009, Cerebral vasospasm following subarachnoid hemorrhage: time for a new world of thought, **Neurological research**, 31.2:151-158.

10 Muroi, Carl, et al., 2012, Novel treatments for vasospasm after subarachnoid haemorrhage, **Current opinion in critical care** 18.2:119-126.

11 Mees SD et al., 2007 Calcium antagonists for aneurysmal subarachnoid haemorrhage, **Cochrane Stroke Group**

12 Hackett ML & Anderson CS., 2000, Health outcomes 1 year after subarachnoid hemorrhage: An international population-based study. The Australian Cooperative Research on Subarachnoid Hemorrhage Study Group, **Neurology** 55:658-662

13 This is calculated based on the estimated incidence of strokes of 795,000 in the U.S., of which 5 per cent are accounted for by SAH and the scaled to estimate the developed-world population.

and the Nrf-2 activator Tecfidera[14]. There are a number of new therapies in development, many of which are immune modulators.

Historical and Forecasted Sales of Tecfidera

		WW Sales ($M)							
Product	**Company**	**2013**	**2014**	**2015**	**2016**	**2017**	**2018**	**2019**	**2020**
Tecfidera	Biogen Idec	876	2,909	3,950	4,754	5,418	5,853	6,165	6,502

Sources: EvaluatePharma consensus estimate based on forecasts from JP Morgan, Morgan Stanley, Credit Suisse and Goldman Sachs. WW sales excluding certain Asian markets.

2.4. Prostate Cancer

Prostate cancer is the most common cancer amongst American men, with increasing risk associated with age, ethnicity and familial history[15]. It is also one of the leading causes of cancer deaths. The World Health Organisation estimates that there were 1.2 million men diagnosed with prostate cancer in 2012, with higher rates of incidence in more developed countries. It is estimated that approximately 307,000 men died from prostate cancer in the same year, with a global prevalence of approximately four million men with prostate cancer.

In the US, surgery is the treatment of choice for men with early-stage prostate cancer who are in good health, which may be supported by radiotherapy. In Europe, active surveillance is much more widely practised for early-stage prostate cancer. Alternatively, older men or those with other health problems often receive radiotherapy, which can include external radiation sources and internal radiotherapy where radioactive seeds are implanted inside the prostate.

Current pharmacotherapy includes the use of hormone therapies utilising luteinising hormone blockers such as Zoladex, gonadotrophin-releasing hormone blockers (Firmagon), anti-androgens such as Xtandi and Casodex, as well as the cytochrome p17 blocker Zytiga. Hormone therapy is usually reserved for later-stage cancers. If hormone therapy does not control the cancer, chemotherapy can be used to treat the malignancy. Chemotherapy drugs used in prostate cancer include docetaxel, mitoxantrone, paclitaxel, epirubicin and estramustine.

A major concern relating to the advent of prostate cancer screening is the rise in administration of aggressive treatment for early-stage (stages I and II) prostate cancers that, if left untreated, may in fact grow very little, or not at all. It is likely that a high proportion of the cases of prostate cancer diagnosed each year are early-stage or low risk cancers.

More recently, men diagnosed with early-stage prostate cancer can opt to engage in active surveillance, whereby the prostate is regularly monitored by physical examination and biopsy. However, there is concern that active surveillance may miss the progression of some cancers towards metastasis[16], although recent long-term studies have shown little or no difference in survival between radical prostatectomy and active surveillance[17]. Further, there is currently no available therapeutic treatment aimed at reducing the risk of prostate cancer progression for men who have elected active surveillance, and some patients elect to undergo prostatectomy or to receive radiotherapy[18]. It is estimated that between 30 – 40 per cent of men who have undergone surgical or therapeutic treatment likely had tumours that would not have become a threat to health or lifespan[19].

The market for prostate cancer treatments is large. According to BCC Research the global market for therapeutics for prostate cancer was estimated to be $8.1 billion in 2012 and to grow rapidly to nearly $18.6 billion in 2017. Although there are no therapeutics approved for the subset of patients being targeted by SFX-01, as many as 30 per cent of prostate cancers may be addressable. Even with relatively modest pricing and penetration rates, chronic treatment with SFX-01 has significant commercial potential.

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14 Datamonitor

15 CDC Prostate Cancer Fact Sheet

16 Indolent prostate cancer and active surveillance, 2010, "http://www.cancerworld.com/Articles/Issues/34/" January-February-2010/e-Grand-Round/363/Indolent-prostate-cancerand-active-surveillance.html

17 Kwon, O., & Hong, S. (2014). *Active surveillance and surgery in localized prostate cancer*. **Minerva urologica e nefrologica** 66(3), 175-187

18 CDC Prostate Cancer Fact Sheets, http://www.cdc.gov/cancer/prostate/basic_info/treatment.htm

19 Prostate Cancer Foundation, http://www.pcf.org/site/c.leJRIROrEpH/b.8968729/k.D255/Improving_methods_to_identify_indolent_versus_aggressive_prostate_cancer.htm

2.5. Chronic Obstructive Pulmonary Disease

Chronic Obstructive Pulmonary Disease is an umbrella term used to describe usually progressive chronic lung diseases that cause limitations in lung airflow, which have historically included 'chronic bronchitis' and 'emphysema'. The most common symptoms of these lung diseases are breathlessness, excessive production of sputum and a chronic cough. The disease is largely induced by lifestyle and environmental influences, and results primarily from inhalation of tobacco smoke, indoor air pollution and various occupational hazards such as dust and chemicals. The primary damage develops as a significant and chronic inflammatory response to environmental irritants, oxidative stress in lung tissues and breakdown of lung tissue by aberrant activity of proteases.

COPD presents a complex medical and economic problem with the WHO predicting that COPD will become the third leading cause of death worldwide by 2030. The incidence of COPD appears to be rising rapidly. According to WHO, 64 million people were affected by COPD in 2004. Consequently, the value of the market for pharmaceutical interventions is high and growing fast, estimated at US$10 billion in 2013 and projected to grow at a CAGR of 7.1 per cent to reach $14.1 billion in 2018[20].

The disease is treated primarily with drugs that dilate the lung airways, sometimes supported with corticosteroids and antibiotics. There are two major types of these inhaled bronchodilators, ß2 agonists and anticholinergics. Approximately 75 per cent of this market is shared between two drugs, Pfizer's Spiriva and GlaxoSmithKline's Advair/Seretide[21].

2.6. Osteoarthritis

Osteoarthritis is a common form of arthritis, affecting millions of people worldwide. Although as many as 250 million people worldwide may be affected by OA, we estimate that the addressable market for SFX-01 is still a substantial 95 million in key commercial markets. The disease is a major cause of disability and hospital admissions: for example, in 2011 it was regarded as the most expensive condition seen in US hospital stays in that year, with an aggregate cost of $14.8 billion.

OA is a degenerative disease of the entire joint involving the cartilage, joint lining, ligaments, and underlying bone. The joints most commonly affected are the knees, hips, and those in the hands and spine. The specific causes of OA are complex, but are believed to be a result of both mechanical stress and molecular events in the affected joint.

Disease onset is gradual, usually beginning after the age of 40, and there is currently no cure for OA. Treatment for OA focusses on relieving symptoms and improving function, and can include a combination of patient education, physical therapy, weight control, use of medications, and eventually, total joint replacement.

Anti-inflammatories and analgesics are the primary pharmaceutical treatments of OA depending on disease severity. Although much of the market is generic, the global osteoarthritis therapeutics market was estimated to be worth $4.4 billion in 2010 and is expected to grow to $5.9 billion with a compound annual growth rate (CAGR) of 3.8 per cent by 2018, according to a 2012 report from GlobalData[22].

3. Sulforadex technology and lead product SFX-01

3.1. Stabilised Sulforaphane

Various members of the Brassica family of vegetables, most notably broccoli, contain glucoraphanin. On cutting or chewing the broccoli, glucoraphanin is broken down (hydrolysed) into sulforaphane by enzymes in either the plant or by bacteria in the digestive tract. In addition to extraction from cruciferous vegetables, chemical routes of synthesis for sulforaphane have now been established.

However, pure sulforaphane is inherently unstable and in its natural liquid form, needs to be stored at -20°C under an inert gas, making the pure form highly unsuitable for use as a pharmaceutical agent. If regular sulforaphane is stored at room temperature, in a sealed container, there is a significant loss of activity after just two to three months. The practical considerations have stymied the clinical development of sulforaphane. The stabilised form of sulforaphane (as manufactured

20 FirstWord Pharma, 2013, *Chronic Obstructive Pulmonary Disorder (COPD)* – KOL Insight and Consensus Outlook

21 *Ibid.*

22 GlobalData 2012, *Osteoarthritis (OA) Therapeutics – Pipeline Assessment and Market Forecasts to 2018*

using the Sulforadex® technology) in a lattice of α-cyclodextrin (embodied in lead product SFX-01, which is a solid powder) represents a significant advance, enabling the development of a pharmaceutical in conventional capsules or pill formats. SFX-01 has been demonstrated in ICH[23] stability studies to maintain stability, and remain within product specification for at least 24 months.

Evgen holds the worldwide exclusive rights to the intellectual property relating to and applications of a synthetic stabilised form of sulforaphane complexed with α-cyclodextrin. Evgen, working with the Licensor, has developed a patent-protected[24], scalable manufacturing process for SFX-01, which the Licensor manufactures, under contract, in their cGMP FDA-accredited manufacturing facility for use in clinical trials. Evgen believes that the process is robust and scalable to shipping the finished pharmaceutical in commercial quantities.

SFX-01 has been shown to have excellent pharmacokinetics, with ability to deliver significant sulforaphane concentrations to the plasma both in animals and man. It has a bioavailability of approximately 80 per cent and a half-life that is comparable to pure sulforaphane. In all *in vitro* and *in vivo* tests undertaken by the Company – including solid tumour cell lines, haematological cell lines and non-cancer animal models (i.e. COPD) – SFX-01 has been shown to be equipotent with regular sulforaphane. Furthermore, in a preclinical industrial-scale screen with a large UK-based research institute, SFX-01 has shown anti-cancer activity in over 900 cancer cell lines.

3.2. Mechanism of Action

In mechanistic terms, the biological activity of sulforaphane appears to be complex and is thought to fall within three pathways that may be related. The primary effect of sulforaphane is the up-regulation of the activity of protective cellular mechanisms and the down-regulation of inflammatory pathways.

Human cells possess a complex mechanism to counteract the deleterious effects of oxidative stress, which result from a disturbance in the normal balance of antioxidant/oxidant homeostasis. This imbalance leads to the abnormal production of reactive oxygen and nitrogen species, which can directly damage cells and may also initiate pro-inflammatory pathways. The cytoprotective and antioxidant enzymes that counteract these reactive species are regulated by a common mechanism that consist of a protein called Keap1[25] and a transcription factor known as Nrf2.

Under normal conditions Keap1 sequesters Nrf2 rendering it biologically inert. However, in situations of oxidative stress, ''sensors'' on the Keap1 protein detect the abnormal conditions and release Nrf2, which promotes the expression of cytoprotective proteins. Nrf2 also inhibits another transcription factor called NF-$_K$B which regulates the expression of inflammatory genes, and has been found to be highly expressed in tissues that are frequently subject to environmental and metabolic stresses such as lung, gastrointestinal tract, liver and kidneys[26]. Currently, Biogen Idec's Tecfidera – indicated for multiple sclerosis – is the only marketed Nrf2 pathway activator.

However, while there are currently few Nrf2 pathway activators in clinical development, they are being increasingly explored as potential treatments across a number of indications in which oxidative stress and inflammation are thought to be a key part of the disease mechanism. Recent studies suggest that the disturbance of normal Nrf2 and NF-kB regulation is implicated in a number of pathologic processes, including obesity and type II diabetes, diabetic neuropathy, neurodegenerative disorders, acute kidney disease and cancer[26, 27, 28, 29, 30]

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23 International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (''ICH'')

24 Patent is in prosecution and has not yet been granted

25 Kelch-like ECH-associated protein 1

26 Zoja, C., Benigni, A., & Remuzzi, G., 2013, *The Nrf2 pathway in the progression of renal disease*, **Nephrology Dialysis Transplantation**, gft224

27 Chartoumpekis, D. V., & Kensler, T. W., 2013, *New player on an old field; the Keap1/Nrf2 pathway as a target for treatment of type 2 diabetes and metabolic syndrome*. **Current diabetes reviews**, 9(2), 137

28 Kansanen, E., Kuosmanen, S. M., Leinonen, H., & Levonen, A. L., 2013, *The Keap1-Nrf2 pathway: Mechanisms of activation and dysregulation in cancer*, **Redox biology**, 1(1), 45-49

29 Ganesh Yerra, V., Negi, G., Sharma, S. S., & Kumar, A., 2013, *Potential therapeutic effects of the simultaneous targeting of the Nrf2 and NF-kB pathways in diabetic neuropathy*, **Redox biology**, 1(1), 394-397

30 Yang, Y., Jiang, S., Yan, J., Li, Y., Xin, Z., Lin, Y., & Qu, Y., 2014, *An overview of the molecular mechanisms and novel roles of Nrf2 in neurodegenerative disorders*, **Cytokine & growth factor reviews**

Selected Nrf2 Pathway Activators in Clinical Development

Company	Product	Indications	Current Development Phase
UCB	Tecfidera	Multiple sclerosis	III
AbbVie/Reata Pharmaceuticals	RTA 408	Radiotherapy-induced side effects, Ocular inflammation, Cataract surgery, Post-operative pain	II
AbbVie/Reata Pharmaceuticals	RTA-ABT 408	Melanoma, Mitochondrial disease, Friedreich's ataxia, Ocular inflammation, Non-small cell lung cancer (NSCLC), Radiotherapy-induced side effects	II
XenoPort	XP23829	Psoriasis, MS, Parkinson's disease	II
InVasc Therapeutics/ BioLink Life Sciences	INV-144	Diabetic nephropathy, Chronic kidney disease (CKD), Hypertension (HTN)	II
Kyowa Hakko Kirin/ Reata Pharmaceuticals	Bardoxolone methyl	Diabetic nephropathy, Chronic kidney disease (CKD), Solid tumour indications, Non-Hodgkin lymphoma (NHL), General cardiovascular indications, Pulmonary hypertension, Other metabolic indications, Melanoma, General liver disorders, Pancreatic cancer	II
Alkermes	ALKS 8700	Multiple sclerosis	I
The Johns Hopkins University	Respiratory Research Program	COAD/COPD	I

[†]UCB is developing Tecfidera for China, South Korea, Hong Kong, Thailand, Singapore, Malaysia & Taiwan
Source: EvaluatePharma

More recently, sulforaphane has been shown to inhibit a group of proteins called histone deacetylases ("HDACs")[31]. Inhibition of these proteins can result in the reactivation of aberrantly silenced tumour suppressor genes, which may induce cell cycle arrest or apoptosis in cancer cells. Sulforaphane has caused a reduction in HDAC activity and down-regulation of select class I and class II HDAC proteins. HDAC inhibition is a well-established target for anti-cancer compounds, and a number of HDAC inhibitors have been approved for marketing or are in late stage clinical studies. HDAC inhibition is also a possible mechanism of action of the well-established neurological drug valproic acid.

31 Clarke, J. D. et al. Comparison of Isothiocyanate Metabolite Levels and Histone Deacetylase Activity in Human Subjects Consuming Broccoli Sprouts or Broccoli Supplement **J. Agric. Food Chem**. 59, 10955-10963 2011.

Selected Marketed and R&D HDAC Inhibitors

Company	Product	Generic Name	Phase
Celgene; Cyclacel Pharmaceuticals	Istodax	romidepsin	Marketed; Filed
Novartis	Farydak	panobinostat	Marketed
Spectrum Pharmaceuticals	Beleodaq	belinostat	Marketed
Merck & Co	Zolinza	vorinostat	Marketed
Shenzhen Chipscreen Biosciences	Epidaza	chidamide	Approved
Bayer; GSK; Syndax Pharmaceuticals; University of Colorado; Eddingpharm	Entinostat	entinostat	Phase III
MEI Pharma	Pracinostat	pracinostat	Phase II
Mirati Therapeutics; Otsuka Holdings	Mocetinostat	mocetinostat	Phase II
Chroma Therapeutics	CHR-2845	tefinostat tartrate	Phase II

Source: EvaluatePharma

Tumours are thought to harbour a very small sub-population of cancer cells – called cancer stem cells – that are capable of initiating tumour formation. Sulforaphane may also have an effect on cancer stem cells via the down-regulation of the Wnt/ß-catenin and sonic hedgehog genes, which are implicated in the control of adult stem cells and certain cancers. Evgen has worked with the Paterson Institute for Cancer Research in Manchester UK to show in a series of different *in vitro* and *in vivo* models (with patient-derived breast tissue) that sulforaphane can target cancer stem cells, suggesting it may have a role complementing conventional cancer therapies.

3.3. Activity in Lead and Other Indications

Cancer Indications

Cancers are complex cellular diseases that arise from normal tissues that have accumulated a number of mutations in critical genes. These changes are frequently caused by a number of internal (genetic) and external (epigenetic) factors. It is generally possible to recognise (at least) three stages of the genesis of a tumour: initiation, promotion and progression.

There is an extensive database of published literature demonstrating that sulforaphane may be an effective chemo-protective agent in cell culture in carcinogen-induced and genetic cancer models, as well as xenograft models of cancer. In these studies, sulforaphane has demonstrated cytostatic and cytotoxic qualities[32].

Sulforaphane is thought to exert its cytoprotective properties through the modulation of Phase I and Phase II enzymes that are active in the initiation phase of carcinogenesis. Many *in vitro* and *in vivo* studies have shown that sulforaphane inhibits Phase I enzymes thereby blocking the initiation of chemically-induced carcinogenesis. It is also a potent inducer of Phase II enzymes that detoxify the cell and protect against carcinogens. Other studies have shown that sulforaphane can counteract the genotoxicity of carcinogenic compounds. This chemo-preventative activity is the basis for its use in early-stage prostate cancers and breast cancers.

Sulforaphane is able to modulate the cell cycle progression of many cellular models of cancer including prostate and breast amongst others, as well as arrest cells in several phases of the cell cycle, such as G1, S and G2/M. This results in cell stasis and inhibits the promotion phase of tumour genesis. The cytostatic effect described immediately above is supplemented by a cytotoxic effect of sulforaphane which has been described in many tumour cell lines including breast and prostate cancer cell lines. The precise mechanism of the cytostatic and cytotoxic effects of sulforaphane have not been fully described and are likely to arise from a broad spectrum of activity across a number of targets.

Epidemiological studies have substantiated an association with high consumption of cruciferous vegetables (particularly broccoli) and a reduction in the risk of various types of cancers. Recent studies have also suggested that sulforaphane can inhibit angiogenesis, the process of forming new blood vessels that allow the tumour to nourish itself, expand, and eventually metastasise. It has also shown some ability to inhibit the conversion of tumours from benign to malignant, as well as reduce metastasis in several *in vivo* models of cancer.

32 Lenzi et al, *Sulforaphane as a promising molecule for fighting cancer* **Treat Res. 2014**

Sulforaphane is also thought to target cancer stem cells, possibly through the Wnt/ß catenin pathway, in several models of cancer including prostate and breast. In addition to the extensive database of published literature, Evgen has established that SFX-01 significantly enhances the activity of tamoxifen against patient-derived early breast cancer cells and metastatic cancer cells. This supports previous findings that sulforaphane independently reduced the size and number of primary mammospheres created by human breast cancer cells[33].

The effects of SFX-01 on breast cancer stem cell activities have been studied in patients samples and Xenograft models, by measuring several markers of stem cell activity including mammosphere formation and aldehyde dehydrogenase levels. SFX-01 has been shown to reduce mammosphere formation efficiency in patient derived samples and reduce activity of breast CSCs in both early and metastatic breast cancer Xenografts. Interestingly both the HBCx34 and BB3RC31 Xenografts lack estrogen receptors. The effects of sulforaphane on ER- breast cancer cells lines has been replicated by an independent research group using a non-stabilised sulforaphane This activity may be important in delaying the onset of resistance, potentially prolonging the efficacy of hormone therapies.

Although the primary oncology indication is breast cancer, there is considerable evidence of the utility of sulforaphane in Prostate cancer. A recent six-month Phase II clinical study with a botanical extract of sulforaphane from Broccoli seeds (Prostaphane™) indicated that it may have a positive long-term effect in the reduction of biochemically relapsing prostate cancer following radical prostatectomy. Although the 90 patient study missed its primary endpoint, secondary endpoints were met and the substantial increase in PSA doubling time may be clinically relevant, particularly when tested across a longer time frame and in a greater number of patients[34]. Similar reductions in PSA doubling time have been observed in earlier clinical trials using sulforaphane extracts[35].

Subarachnoid Haemorrhage

A secondary component of the morbidity associated with SAH is due to secondary injury from inflammation, spreading depolarisation, macroscopic cerebral vasospasm and microcirculatory disturbance. A common factor in all these mechanisms is initiation by the presence of extracellular haemoglobin, which is released from red blood cells after haemorrhage. As well as direct neurotoxicity, the extracellular haemoglobin increases oxidative stress, and thereby further injury.

Nrf2, which is up-regulated by sulforaphane, is a promoter of haptoglobin expression, as well as a wide range of antioxidant and anti-inflammatory enzymes including Heme Oxygenase-1 (“HO-1”) and NAD(P)H:quinone oxidoreductase-1 (“NQO1”). Haptoglobin is part of the normal haemoglobin clearance pathway, binding free haemoglobin with extremely high affinity and thereby inhibiting its oxidative activity. The administration of sulforaphane has been shown to reduce inflammation and neurological deficits in rats after intracerebral haemorrhage[36] and subarachnoid haemorrhage. Indeed, Nrf2 deficient mice are significantly more prone to the neurological deficits of haemorrhagic brain injury. Sulforaphane is thought to be capable of penetrating the blood-brain barrier, with at least one study suggesting significant accumulation of sulforaphane in cerebral tissue and several models of acute neurodegeneration demonstrating the neuroprotective effects of sulforaphane[37].

The Nrf2 mechanism of action is already validated in an inflammatory disease of the central nervous system, with a commercially approved drug, Tecfidera, which is approved for the treatment of relapsing-remitting multiple sclerosis.

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33 Li et al., Sulforaphane, a Dietary Component of Broccoli/Broccoli Sprouts, Inhibits Breast Cancer Stem Cells **Clin Cancer Res.** 2010 16(9): 2580-2590.

34 Cipolla et al.,Effect of Sulforaphane in Men with Biochemical Recurrence after Radical Prostatectomy **Cancer Prevention Research** Prostaphane™ study – SF & DH is this published yet?

35 Alumkal et al., Sulforaphane treatment in men with recurrent prostate cancer, **J Clin Oncol** 31, 2013 (suppl;abstr 5017)

36 Zhao et al., Transcription Factor Nrf2 protects the brain from damage produced by intracerebral haemorrhage, **Stroke 2007**

37 Tarozzi, Andrea, et al., 2013, Sulforaphane as a potential protective phytochemical against neurodegenerative diseases, **Oxidative medicine and cellular longevity**

Other Indications

In a mouse model of spontaneous osteoarthritis (STR/ort mice), treatment with SFX-01 has been shown to significantly improving bone architecture by increasing bone mass and strength, but without modifying joint osteoarthritis score. Treatment also improved osteoarthritis associated gait asymmetry. Combined with the observed reductions in cartilage damage and osteoarthritis in another experimental model of OA[38], the osteotrophic effect of SFX-01 in this model highlights its potential as a novel treatment for osteoarthritis.[39]

3.4. License with PharmAgra and Lalilab

In 2010, Evgen entered into an Option Agreement to license, on a worldwide exclusive basis, the intellectual property and know-how embodied in SFX-01 by PharmAgra Labs Inc. (North Carolina) and Lalilab Inc. (North Carolina). The option was exercised in 2011 and the license was subsequently modified in 2013 to recover the commercial manufacturing rights. The final license terms included a carve-out of the topical applications (with the exclusion of skin cancer application), which are retained by the Licensors. The principal terms include very modest clinical development milestones, regulatory approval milestones and a royalty rate consistent with certain other enabling technologies. These are summarised below:

Payment	**Amount ($)**
Clinical development milestones	$250,000
Regulatory approval milestones	Up to $6,000,000 in regulatory filing and grant milestones
Royalty on own sales	Up to 3.5 per cent of net sales
Sub-licensing	Between 10 per cent and 25 per cent of sub-license revenues depending on circumstances of the sub-license

We believe that the deal struck with the Licensors for the Sulforadex® technology is commercially reasonable and will not impede the sub-licensing of the product to any future partner, should Evgen elect to do so. In the event that 75 or more patients are recruited in any combination of trials, then the sub-licensing royalty will settle at the lowest level of 10 per cent. Evgen expects to achieve this in the first 14 months after the proposed IPO on the AIM market of the London Stock Exchange and in the event that it recruits 50 patients, the patent estate is assigned to Evgen.

3.5. Manufacturing

Evgen has an exclusive contract with PharmAgra for the bulk supply of stabilised sulforaphane (i.e. the active ingredient in SFX-01) for clinical trial purposes. Sulforaphane is manufactured using a simple three-stage synthesis from readily available starting materials such as Erucin, and is concurrently complexed *in situ* with α-cyclodextrin to form SFX-01. Evgen intends to transfer the manufacturing to a larger partner for commercial scale, and the clinical trial supply manufacturing agreement is constructed to facilitate this transfer.

Evgen intends to formulate SFX-01 in two distinct product formats: a capsule and a solid tablet format. The capsule formulation will be used in the subarachnoid haemorrhage indication, whilst tablets will be tested for the longer-term treatment indications. These differences, amongst others, may allow Evgen or a partner to establish differential pricing for different indications.

Long-term stability data are an important pre-requisite of the regulatory process and recent stability data from studies conducted by third parties demonstrate the stability of SFX-01 to ICH standards over a two-year timeframe. The current stability data is sufficient for clinical trial purposes, and we would expect additional stability data to be developed as the drug progresses through clinical trials. In addition to other protections, Evgen has filed intellectual property relating to the manufacturing process for SFX-01.

Using the active pharmaceutical ingredient manufactured by PharmAgra, Evgen has retained the services of a contract manufacturing company, PharMaterials, to produce clinical trial supplies of SFX-01 capsules for its SAH trial. In the SAH trials, SFX-01 may be administered to patients unable to take the drug orally via a nasogastric tube, which will involve releasing the contents of SFX-01 capsules into saline in the hospital environment.

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38 Davidson, R et al. ,2013 *Sulforaphane Represses Matrix-Degrading Proteases and Protects Cartilage From Destruction In Vitro and In Vivo*, **Arthritis and Rheumatism**, pages 3130-3140)

39 Javaheri et al., ECTS 2015 poster and unpublished data

4. Preclinical and Clinical Development

4.1. Preclinical Safety

Although there is a long history of consumption by humans of the pre-cursor molecule glucoraphanin in normal diet, and an extensive database of the clinical use of sulforaphane derived from botanical sources, SFX-01 is a synthetic product that has had to undergo a full toxicology and safety pharmacology programme.

The extensive preclinical safety package compiled thus far for SFX-01 suggests that no safety risks were identified in the cardiovascular, central nervous system and respiratory systems. A panel of genetic toxicology studies did not identify any genetic toxicological risks (Ames Test and an *in vivo* chromosomal aberration studies). SFX-01 was well tolerated in 28-day repeat-dose studies in rats and primates up to a dose of 65mg/kg in primates. The principal toxicities affected the urinary bladder and gastrointestinal tract, but were fully reversible. Those observed were considered minor and did not prevent the regulatory authorities granting Evgen permission to conduct clinical studies healthy human subjects.

4.2. Chronic Safety and Toxicology Programme

Additional safety and toxicological studies will be conducted through the development of SFX-01. These clinical trials require short-term exposure to SFX-01, for which the current safety and toxicology programme is adequate. The additional toxicology studies are required for the Phase II clinical studies, which require a more prolonged exposure to drug. Evgen or a partner will also have to conduct reproductive system toxicology tests in both male and female subjects. We expect standard carcinogenicity testing to also be required in due course for longer-term treatment in the oncology indications, while fertility studies will be required to treat female patients of child bearing age.

4.3. Completed Clinical Studies

Evgen has conducted two clinical studies that have established the safety and tolerability profile of SFX-01 in man. Although minor side effects were observed in the first study, these findings allowed Evgen to optimise the presentation (adding enteric coating) and refine the dosing regimen by splitting the dose into a twice-daily administration. In the second trial, these improvements eliminated the side-effects seen with the single dosing regimen.

Phase I SAD Trial

The Phase I Single Ascending Dose (“SAD”) study consisted of a randomised, double-blind, placebo-controlled study with single ascending doses of SFX-01 administered to healthy male subjects between 18 to 45 years of age. Twenty nine (29) healthy male subjects completed the study and were analysed in a total of five cohorts. Each cohort consisted of healthy subjects either on placebo or the active substance (SFX-01) at five different dose levels (50mg, 100mg, 300mg, 500mg and 700mg). Subjects remained in-house for two days and were followed up 7-14 days after discharge. Safety monitoring and serial blood samples for PK evaluation were taken through the period of admission.

The study concluded that oral doses up to 300mg SFX-01 were safe and tolerated by the majority of subjects. There were no significant adverse events and no subjects withdrew from the study due to treatment emergent adverse events, or for any other reason. The majority of treatment emergent adverse events were of mild intensity, and four treatment emergent adverse events were of moderate intensity (vomiting and abdominal pain). Increased frequency of vomiting was observed as the dose was increased to 500mg and 700mg, but these effects were short-lived and were entirely absent within two-hours post dose.

No clinically-significant changes were observed in a battery of clinical laboratory tests, physical examinations, vital signs, Holter ECGs, telemetry and 12-lead ECG parameters.

Phase I MAD Trial

The Phase I multiple ascending dose (“MAD”) study was a randomised, double-blind, placebo-controlled design to evaluate the safety, tolerance, PK and PD of multiple doses of SFX-01 administered once daily (“qd”) or twice daily (“bid”) in healthy male subjects following dosing for seven days. A total of 18 subjects were enrolled in three equally-sized cohorts with four subjects on active drug and two on placebo. Two different dosing regimens were tried: 600mg once daily or 300mg twice daily. The subjects received drug or placebo every day for a period of seven days.

The two cohorts receiving 600mg once daily were either fed or fasted. Subjects were admitted to the clinical pharmacology unit on day 1 and remained in-house until day 9. A follow-up visit was performed 7-14 days after discharge.

Oral doses of 600mg once daily and 300mg bid were safe and well tolerated by the majority of subjects, with no serious adverse events observed. No subjects withdrew due to adverse events. All adverse events were of mild intensity except for three moderately intense adverse events, and were all in the once daily cohort. There were no clinically significant changes in clinical laboratory safety tests, physical examinations, vital signs, telemetry and 12-lead ECG parameters.

4.4. Planned Studies

Preclinical Xenograft Studies

The proposed Xenograft studies involve the engraftment of human cancer tissues into mice to simulate the progression of the human disease. Xenograft models have been developed for both hormone sensitive and endocrine therapy resistant clinical samples. These models will be used to evaluate SFX-01 in primary and secondary resistance settings, alone and in combination with established breast cancer drugs, tamoxifen and fulvestrant. These studies will provide information on any potential synergies SFX-01 may have, as well as longer-term data on the retardation of tumour growth.

Phase IIa/IIb Breast Cancer Study

In parallel with the Xenograft Studies, Evgen intends to conduct a Phase IIa/IIb study that will examine the effect of adding SFX-01 to a commonly used second-line therapy fulvestrant (Faslodex) on the progression free survival of post-menopausal patients with ER+ metastatic breast cancer. The patients enrolled in this trial will have failed on prior adjuvant (post-surgical) or first line aromatase inhibitor therapy.

The trial is structured such that if the Phase IIa component succeeds, the number of patients treated will expand from the initial 40 to 200 in total for the P2B. The primary endpoint of the Phase IIa component will be the percentage change in tumour size from baseline. If certain pre-specified efficacy criteria are met and the treatment considered tolerable, the trial will be expanded into the Phase IIb component. A further 160 patients will be enrolled in a randomised, open label, parallel group study. The outcomes of the study will be measured using RECIST 1.1 criteria to evaluate disease progression and the primary analysis will be performed after a pre-specified number of progression free survival events. Secondary endpoints in the Phase IIb include objective response rate, duration of response, and overall survival, as well as safety and toxicity.

With progression free survival being a meaningful and recognised clinical end point in breast cancer, the study could be considered supportive of primary efficacy for an NDA submission.

Phase II Subarachnoid Haemorrhage Study

In conjunction with Southampton NHS Foundation Trust and a second clinical site, Evgen is planning to conduct a Phase II study of the effects of SFX-01 in subarachnoid haemorrhage. The randomised double blind single-centre clinical study will involve approximately 90 subjects who present within 48 hours of ictus. The subjects will be randomised to drug or placebo and will receive oral treatment for 28 days twice daily after presentation. Patients on drug will receive 600mg SFX-01 per day, administered in two 300mg capsules 12-hours apart. As seen in the Phase I MAD study, the twice-daily dosing regimen demonstrated no side effects.

The primary endpoints of the study will be a reduction in trans-cranial Doppler velocity following subarachnoid haemorrhage to determine the effect of sulforaphane on cerebral vasospasm and a functional measure of efficacy such as the Glasgow Coma Scale. Secondary endpoints will be determining increases in plasma and CSF levels of sulforaphane, serum haptoglobin, a reduced incidence of delayed cerebral ischaemia, reductions in iron deposition and cortical atrophy, and improvements in long-term outcomes.

4.5. Planned Preclinical Efficacy Study in MS

Experimental autoimmune encephalomyelitis (‘‘EAE’’) is one of the most widely used animal models of MS. Evgen is planning to test SFX-01 in two well established variants of the EAE model that will allow study of its drug in several phases of EAE that correspond to different stages of the course of the human disease of MS. These include the relapsing phase, the conversion from relapsing to progressive phase and the progressive phase itself.

Two different doses of SFX-01 will be administered: equivalent to 300mg twice daily and 150mg twice daily in humans. As an active comparator, the active ingredient in Tecfidera (dimethyl fumarate) will be administered to a separate cohort of animals. This agent is already approved for use in humans suffering from MS and has been shown to be effective in animal models such as EAE. Including a control arm, the study will comprise a total of four cohorts of animals. The read-outs from this study may be used as the foundation for additional preclinical studies that define the mechanism of action and potentially human clinical trials with SFX-01 in MS.

4.6. Additional Products

Under an agreement with the University of Seville and the Spanish CSIC (Consejo Superior de Investigaciones Científicas), Evgen has an option over rights to next generation sulforaphane analogues. Evgen is in the early stages of testing two equipotent isomers of one analogue produced by this programme that has been observed to enhance Nrf2 activity *in vitro* and *in vivo*. It is expected that these analogues display differential activity from native sulforaphane and may facilitate further segmentation of the markets in oncology, neurology and other inflammatory diseases.

5. Route to Market

Evgen, or a partner, will need to conduct further clinical studies to gain approval of SFX-01 in all of its chosen indications, the design of which will be informed by the current batch of planned studies. The future development and registration of the breast cancer indication will be dependent on the results on the Phase IIa/IIb multi-site trial. If successful, the Phase IIb component of this study is likely to lead to a Phase III programme that can support registration in key markets[SW1].

Orphan drug designation may be achievable for the use of SFX-01 in SAH. Evgen has begun to prepare a US and EU application for Orphan Drug [SW2]Designation, but will require the results of the Phase II study demonstrating a benefit of the drug, before it can complete a submission for orphan drug status. The primary endpoints from this study (transcranial Doppler measurements) are considered suitable for registration purposes.

6. Risks

Based on the review presented earlier in this report, PharmaVentures has identified key risk factors relating to the development of SFX-01, and a number of risk factors that are general to the biopharmaceutical industry.

Evgen is adopting a portfolio strategy towards clinical development of SFX-01. As with all new drugs in development there is significant risk that SFX-01 will not gain regulatory approval for some or all of the proposed indications for which it is being developed. In general, the probability of gaining regulatory approval is lower for earlier stage indications than those that are more mature in their development. Until the completion of clinical trials that successfully demonstrate the efficacy of SFX-01 in these indications, there remains a risk that they will fail to show the necessary standards of safety and efficacy required for approval by regulatory authorities.

Where compared, SFX-01 has been shown to be equipotent to natural sulforaphane. Despite this assurance, the clinical trials strategy relies, in part, on data from studies that have been conducted in vitro and in vivo using botanically derived and synthetic sources of sulforaphane.

The regulatory pathway for adjunctive drugs in subarachnoid haemorrhage is not entirely established, and despite the evident need for effective pharmaceuticals in this indication, the pathway to regulatory approval in key commercial markets may be more complex than envisaged. Regulatory pathways are subject to change, which may or may not benefit the development of SFX-01 in its target indications. In comparison, the regulatory pathway for a second-line approval in breast cancer is well understood.

Although Evgen has developed a cGMP manufacturing process for its clinical trial programme based on the relatively simple synthesis and complexing of its constituent parts, and the Company has scaled this manufacture to kg batches, there is no guarantee that the Company can easily scale the manufacturing process to commercial volumes of sufficiently stable material. Any failure or delay to the manufacture of its products may affect the clinical trial, regulatory and commercial aspects of SFX-01.

Even if successfully developed and authorised by regulatory bodies, there can be no certainty over the commercial success of SFX-01 in the proposed indications. Even if regulatory approval is

obtained, reimbursement by payers will also be needed to make the product a commercial success.

Although Evgen has selected indications where there is little competition from existing or pipeline pharmaceuticals, there remains a risk that its competitors may develop new products which could compete with SFX-01, and may reduce the commercial potential of Evgen's product. Additionally, alternative methods of stabilising synthetic or extracted sulforaphane may be developed which if approved, provide competition to SFX-01.

Following the admission of Evgen to the AIM Market of the London Stock Exchange, the level and complexity of activities at Evgen is likely to increase, especially with respect to the clinical development of SFX-01. This may create an increased requirement for experienced managerial resources in other areas such as finance, research and development, regulatory, manufacturing and business development. Evgen fully appreciates this and is taking steps to strengthen its executive team by way of the appointment of John Bradshaw as Finance Director, and a Chief Medical Officer and a regulatory consultant will be appointed after the IPO. Searches to identify suitable candidates are already underway.

Evgen does not currently possess all the resources required to develop SFX-01 in all its oncology indications through to regulatory approval in key commercial territories. It is, however, possible that in subarachnoid haemorrhage, the Company could gain a conditional approval as early as 2018 if orphan drug designation is secured and the clinical benefits are significant. If it fails to secure a partner, through licensing or similar activities, or secure additional resources, Evgen may not be able to exploit the full commercial value of SFX-01, or may have to raise additional capital.

7. Conclusions

The potential of SFX-01 as a cytoprotective pharmaceutical is underscored by the broad spectrum of activity of sulforaphane across a wide variety of *in vitro* and *in vivo* models of disease, coupled with epidemiological studies that have substantiated an association with high consumption of cruciferous vegetables (i.e. broccoli) and a reduction in the risk of various types of cancers. The mechanism of action appears to be effected through several validated disease targets, and its action across multiple mechanisms may have advantage over single-drug, single-target therapeutics.

By stabilising sulforaphane in α-cyclodextrin, Evgen has already overcome one of the major challenges in turning sulforaphane into a commercially useful pharmaceutical. ICH-compliant data from 24-month stability testing support the case for an approvable formulation of SFX-01. Early clinical studies designed to test safety and begin establishing the clinical pharmacology have suggested SFX-01 is well tolerated within the range of predicted effective doses.

Evgen is taking a portfolio approach to its clinical development strategy, targeting a number of serious diseases that have the potential for multi-billion dollar markets. In each of these markets there remain distinct unmet clinical needs, and there is therefore significant commercial potential for a drug with a profile like SFX-01.

As such, the major challenge for Evgen in the medium-term is to translate the promise of widespread preclinical and clinical studies with botanical and synthetic extracts of sulforaphane into clinically-meaningful results with its SFX-01 drug. The proposed uses of this agent in the planned clinical studies for prostate cancer, breast cancer and subarachnoid haemorrhage appear to be well supported by the available literature on preclinical *in vivo* and *in vitro* work, the epidemiological studies in man with plant-derived extracts, as well as the work conducted by Evgen and its collaborators.

Accordingly, should the clinical trial programmes yield clinically-meaningful results, there will undoubtedly be interest from third parties with the resources and expertise to successfully complete the development of and commercialise SFX-01.

Yours faithfully,

PharmaVentures Limited

PART VI

ADDITIONAL INFORMATION

1. RESPONSIBILITY

1.1 The Company and the Directors (whose names appear on page 5 of this document) each accept responsibility individually and collectively for the information contained in this document, including individual and collective responsibility for compliance with the AIM Rules for Companies. To the best of the knowledge and belief of the Directors and the Company, who have taken all reasonable care to ensure that such is the case, the information contained in this document is in accordance with the facts and does not omit anything likely to affect the import of such information.

1.2 The business address of each Director is the registered office of the Company which is set out, together with their respective functions, on page 5 of this document.

2. THE COMPANY

2.1 The Company was incorporated in England and Wales under the Act on 2 October 2014 as a private company limited by shares under the name ''Evgen Pharma Limited'' with registered number 09246681.

2.2 On 14 October 2015, the Company was re-registered as a public limited company under the Act and its name was changed to ''Evgen Pharma plc''.

2.3 On 12 October 2015, the Company adopted the Articles, conditional upon Admission, in substitution for the Existing Articles.

2.4 The issued share capital of the Company as at the date of this document is £134,879.86, comprising those shares which are set out in the table at paragraph 4.3 of this Part VI, each of which are fully paid. The par value of each Ordinary Share is £0.0025. On Admission, the issued share capital of the Company will be £182,177.16, comprising 72,870,862 Ordinary Shares, each of which will be fully paid.

2.5 The liability of the Shareholders is limited. The principal legislation under which the Company was formed and operates is the Act and the regulations made thereunder.

2.6 The registered office and head office of the Company is at Liverpool Science Park Innovation Centre 2, 146 Brownlow Hill, Liverpool, Merseyside L3 5RF and its telephone number is +44 (0) 151 705 3532.

2.7 The Company's web site address is www.evgen.com.

3. THE GROUP

3.1 The Company is the holding company of the Group, which comprises the Company and its wholly owned subsidiary Evgen Limited (''Evgen''), a company incorporated in England and Wales as a private company limited by shares with registered number 06403643.

3.2 At the date of this document, the Company has no other interest in any company, save for Evgen.

3.3 The Group's principal activity is the development of pharmaceutical products.

4. SHARE CAPITAL OF THE COMPANY

4.1 There have been the following changes to the share capital of the Company between the date of incorporation and the date of this document:

4.1.1 on incorporation one ordinary share of £2.00 was subscribed by and issued to Stephen Franklin;

4.1.2 on 5 December 2014, 12,595 ordinary shares of £2.00 each, 18,849 ordinary A shares of £2.00 each and 5,017 ordinary B shares of £2.00 each in the capital of the Company were allotted and issued to the shareholders of Evgen at that time (being now the shareholders of the Company as at the date of this document) pursuant to the Share for Share Exchange Agreement referred to in paragraph 10.3 of this Part VI;

4.1.3 on 26 August 2015, 9,569 ordinary shares of £2.00 each were allotted to subscribers procured by Acceleris at £209 per share pursuant to the Pre-IPO Round as referred to in paragraph 10.19 of this Part VI; and

4.1.4 pursuant to resolutions passed by the shareholders of the Company on 12 October 2015:

(a) each ordinary share of £2 each in the share capital of the Company was sub-divided into 800 Ordinary Shares;

(b) each A ordinary share of £2 each in the share capital of the Company was sub-divided into 800 A Shares; and

(c) each B ordinary share of £2 each in the share capital of the Company was sub-divided into 800 B Shares,

such shares having the same rights and being subject to the same restrictions as set out in the Existing Articles (the "**Sub-division**"), resulting in there being 17,732,000 Ordinary Shares, 15,079,200 A Shares and 4,013,600 B Shares in issue.

4.2 It is expected that the following changes to the share capital of the Company will happen after the date of this document and conditional on Admission:

4.2.1 pursuant to the terms of the 2013 Loan Note Instrument and the 2014 Loan Note Instrument (each as referred to in paragraphs 10.13 to 10.16 of this Part VI respectively), 6,553,330 A Shares will be issued upon the conversion of 2013 Notes and 2,796,895 Ordinary Shares will be issued upon the conversion of 2014 Notes in connection with the Conversion as referred to in paragraph 4.8.5 of this Part VI;

4.2.2 pursuant to the Existing Articles, 7,776,918 Ordinary Shares will be issued in connection with the Bonus Issue as referred to in paragraph 4.8.6 of this Part VI;

4.2.3 all A Shares and B Shares in issue (following the Conversion and Bonus Issue), being 21,632,530 A Shares and 4,013,600 B Shares, will be re-designated on a one-for-one basis into 25,646,130 Ordinary Shares in connection with the Re-designation as referred to in paragraph 4.8.7 of this Part VI, resulting in 53,951,943 Ordinary Shares being in issue immediately prior to Admission; and

4.2.4 18,918,919 Ordinary Shares will be issued in connection with the Placing pursuant to the Placing Agreement as referred to in paragraph 10.5 of this Part VI, resulting in 72,870,862 Ordinary Shares being in issue on Admission.

4.3 The issued share capital of the Company (i) as at the date of this document, (ii) immediately prior to Admission and (iii) as it is expected to be immediately following the Placing and Admission is as follows:

As at the date of this document			Immediately prior to Admission*		Immediately following the Placing and Admission	
Number of fully paid shares	**Class of share**	**Aggregate nominal value (£)**	**Number of fully paid Ordinary Shares**	**Aggregate nominal value (£)**	**Number of fully paid Ordinary Shares**	**Aggregate nominal value (£)**
17,732,000	Ordinary Shares	44,330	53,951,943	134,879.86	72,870,862	182,177.16
15,079,200	A Shares	37,698	—	—	—	—
4,013,600	B Shares	10,034	—	—	—	—

* Includes shares issued upon the Conversion (details of which are set out in paragraph 4.8.5 of this Part VI) and the Bonus Issue (details of which are set out in paragraph 4.8.6 of this Part VI), but excludes the Ordinary Shares to be issued in connection with the Placing.

4.4 The Ordinary Shares have attached to them full voting, dividend and capital distribution (including on winding up) rights, but do not confer any rights of redemption, and are currently subject to the rights and restrictions set out in the Existing Articles, and upon Admission will be subject to the rights and restrictions set out in the Articles which are summarised in paragraph 5 of this Part VI.

4.5 Otherwise than set out in this document, no more than 10 per cent. of the issued share capital of the Company has been paid for with assets other than cash during the period of the financial information set out in Part III of this document.

4.6 As at the date of this document, Company Options are outstanding over a total of 6,991,200 Ordinary Shares at exercise prices of between £0.00875 and £0.10615. It is proposed that following Admission, 1,457,418 Warrants will be outstanding over 1,457,418 Ordinary Shares at a price of £0.37, being the Placing Price. Further details of the Company Options and the Warrants are set out in paragraphs 12 and 10.8 of this Part VI respectively.

4.7 On 25 June 2015, the Company assumed the rights and obligations of Evgen with respect to the Loan Notes, whereby upon a conversion of the Loan Notes, A Shares and Ordinary Shares will be issued in the Company rather than Evgen as referred to in paragraphs 10.14 and 10.17 of this Part VI;

4.8 On 12 October 2015, resolutions were passed by Shareholders and/ or Directors pursuant to which:

4.8.1 the Company was re-registered as a public company limited by shares under the Act under the name of Evgen Pharma plc (the ''**Re-registration**'') and the words ''Public Limited Company'' or the letters ''PLC'' (either in upper or lower case and with or without full stops) were substituted for the word ''Limited'' in the name of the Company and in the Existing Articles;

4.8.2 conditional on the Re-registration:

(a) each ordinary share of £2 each in the share capital of the Company was sub-divided into 800 Ordinary Shares;

(b) each A ordinary share of £2 each in the share capital of the Company was sub-divided into 800 A Shares; and

(c) each B ordinary share of £2 each in the share capital of the Company was sub-divided into 800 B Shares,

such shares having the same rights and being subject to the same restrictions as set out in the Existing Articles (the ''Sub-division'');

4.8.3 conditional on the Re-registration and subject to the Placing Agreement being entered into, the Directors were unconditionally authorised in accordance with section 551 of the Act to allot shares and to grant rights to subscribe for or to convert any security into shares in the Company:

(a) up to an aggregate nominal amount of £23,375.56 in connection with the Conversion referred to in paragraph 4.8.5 of this Part VI;

(b) up to an aggregate nominal amount of £19,442.30 in connection with the Bonus Issue referred to in paragraph 4.8.6 of this Part VI;

(c) up to an aggregate nominal amount of £3,643.54 in connection with the issue of the Warrants;

(d) up to an aggregate nominal amount of £47,297.30 in connection with the Placing; and

(e) otherwise than pursuant to the authorities referred to in paragraphs 4.8.3(a) to 4.8.3(d) (inclusive) of this Part VI, up to an aggregate nominal amount of £60,725.72, being approximately one-third of the issued share capital of the Company following completion of the Placing and Admission;

such authority expiring (unless previously renewed, revoked, varied or extended) on the earlier of (a) the conclusion of the next annual general meeting of the Company and (b) the date which is 15 months from the date of the resolution;

4.8.4 conditional on Re-registration and subject to the Placing Agreement being entered into, the Directors were given the power to allot equity securities (as defined by section 560 of the Act) of the Company as if section 561 of the Act did not apply to any such allotment, such power being limited to:

(a) the allotment of up to 37,503,484 Ordinary Shares in connection with the Conversion referred to in paragraph 4.8.5 of this Part VI, the Bonus Issue referred to in paragraph 4.8.6 of this Part VI and the Placing including the allotment of 1,457,418 Warrants; and

(b) the allotment (otherwise than pursuant to the power referred to in paragraph (a) above) of equity securities up to an aggregate nominal value of £18,217.72 (being approximately ten per cent. of the issued share capital of the Company following completion of the Placing and Admission),

such power expiring (unless previously renewed, revoked, varied or extended) on the earlier of (a) the conclusion of the next annual general meeting of the Company and (b) the date which is 15 months from the date of the resolution.

4.8.5 conditional upon Admission, (i) the 2013 Notes (including all interest thereon) will be converted into A Shares at a price of £0.185 per share, being a 50 per cent. discount to the Placing Price on the basis of 5,405 A Shares for every £1,000 in nominal value of 2013 Notes (excluding the interest thereon), and (ii) the 2014 Notes (including all interest thereon) will be converted into Ordinary Shares at a price of £0.296 per share, being a 20 per cent. discount to the Placing Price on the basis of 3,378 Ordinary Shares for every £1,000 in nominal value of 2014 Notes (excluding the interest thereon) (the "**Conversion**") pursuant to the terms of the 2013 Loan Note Instrument and the 2014 Loan Note Instrument respectively as referred to in paragraphs 10.13 and 10.16 of this Part VI, resulting in the issued share capital of the Company being £115,437.56, divided into 20,528,895 Ordinary Shares, 21,632,530 A Shares and 4,013,600 B Shares;

4.8.6 conditional upon Admission, the sum of £19,442.30 being part of the share premium account of the Company will be capitalised and appropriated as capital to the holders of A Shares and B Shares and the Directors will be authorised to automatically apply such sum in paying up in full 7,776,918 Ordinary Shares and to allot and issue such new Ordinary Shares, credited as fully paid up, to the holders of such A Shares and B Shares (the "**Bonus Issue**"), resulting in the issued share capital of the Company being £134,879.86, divided into 28,305,813 Ordinary Shares, 21,632,530 A Shares and 4,013,600 B Shares;

4.8.7 conditional upon the Re-registration and Admission, each issued A Share and each issued B Share will be re-designated as one Ordinary Share having the rights and being subject to the restrictions set out in the Articles (the "**Re-designation**"), resulting in the issued share capital of the Company being £134,879.86, divided into 53,951,943 Ordinary Shares; and

4.8.8 conditional upon Admission, the Company will adopt the Articles in substitution for and to the exclusion of the Existing Articles.

4.9 Save as disclosed in this document, since 2 October 2014 (being the date of incorporation of the Company):

4.9.1 no share or loan capital in the Company is under option or is the subject of an agreement, conditional or unconditional, to be put under option;

4.9.2 no share or loan capital of the Company has been issued, or is now proposed to be issued, fully or partly paid, either for cash or other consideration to any person;

4.9.3 no person has any preferential subscription rights for any share capital of the Company;

4.9.4 no commissions, discounts, brokerages or other special terms, have been granted by the Company in connection with the issue or sale of any share or loan capital of the Company;

4.9.5 the Company does not hold any of its own Ordinary Shares and the Company's sole subsidiary, Evgen, does not hold any of the Ordinary Shares;

4.9.6 the Company has no securities not representing share capital, convertible debt securities, exchangeable debt securities or debt securities with warrants in issue; and

4.9.7 there are no acquisition rights or obligations over the unissued share capital of the Company and there is no undertaking to increase the share capital of the Company.

4.10 The Ordinary Shares have been created under the Act.

4.11 The Company does not have an authorised share capital.

4.12 The Ordinary Shares have a nominal value of £0.004, are in registered form and may be held either in certificated form or in uncertificated form through CREST. The Articles permit the Company to issue shares in uncertificated form.

4.13 No shares of the Company are currently in issue with a fixed date on which entitlement to a dividend arises and there are no arrangements in force whereby future dividends are waived or agreed to be waived.

4.14 Save for the Company Options and the Loan Notes, at the date of this document the Company does not have in issue any securities not representing share capital. Following Admission, 1,457,418 Warrants will be in issue (further details of which are set out in paragraph 10.8 of this Part VI).

4.15 There are no shares in the capital of the Company which are not fully paid.

4.16 None of the Ordinary Shares have been marketed or are being made available to the public in whole or in part in conjunction with the application for Admission.

4.17 Neither the Ordinary Shares nor any other shares of the Company that have previously been in issue have been admitted to dealing on any recognised investment exchange or other trading facility, nor has any application for such admission been made and it is not intended to make any arrangements for dealings in the Ordinary Shares on any such exchange other than the application to be made in connection with Admission.

4.18 The Company has the contractual capacity of a natural person and is empowered to borrow guarantee and give security.

5. ARTICLES

The Articles (which will apply from Admission) include provisions to the following effect:

5.1 ***Objects***

The Articles contain no restriction on the objects of the Company.

5.2 ***Capital structure***

The share capital of the Company is represented by an unlimited number of Ordinary Shares having the rights described in the Articles. Under the Articles, any share may be issued with such rights or restrictions as the Company may by ordinary resolution determine, or in the absence of such determination, or so far as any such resolution does not make specific provision, as the board may determine.

5.3 ***Variation of class rights***

Whenever the capital of the Company is divided into different classes of shares, the rights attached to any class of the shares in issue may from time to time be varied or abrogated, whether or not the Company is being wound up, with the sanction of a special resolution passed at a separate meeting of holders of the issued shares of the class held in accordance with the Articles (but not otherwise).

The special rights conferred on the holders of any shares or class of shares shall, unless otherwise provided by the Articles or the terms of issue of the shares concerned, be deemed to be varied by a reduction of capital paid up on those shares but shall be deemed not to be varied by the creation or issue of further shares ranking *pari passu* with them or subsequent to them. The rights conferred on the holders of shares shall be deemed not to be varied by the creation or issue of any further shares ranking in priority to them nor shall any consent or sanction of the holders of Ordinary Shares be required to any variation or abrogation effected by a resolution on which only the holders of Ordinary Shares are entitled to vote.

5.4 ***Voting rights***

Subject to any rights or restrictions attached to any shares, on a show of hands every member who (being an individual) is present in person or by proxy or (being a corporation) is present by a duly authorised representative, not being himself a member entitled to vote, shall have one vote, and on a poll every member shall have one vote for every Ordinary Share of which he is the holder.

5.5 ***Dividends***

Subject to the Act and as set out in the Articles, the Company may by ordinary resolution declare dividends but no dividend shall exceed the amount recommended by the Board. No dividend may be paid otherwise than in accordance with the Act. The Board may at any time declare and pay such interim dividends as appears to be justified by the position of the Company.

Except as otherwise provided by the rights attached to the shares, all dividends shall be declared and paid according to the amounts paid up on the nominal amount of the shares on which the dividend is paid but (for the purposes of this Article only) no amount paid on a share in advance of calls shall be treated as paid on the share. All dividends shall be apportioned and paid proportionately to the amounts paid up on nominal amount of the shares during any portion or portions of the period in respect of which the dividend is paid; but, if any share is issued on terms providing that it shall rank for dividend as from a particular date, that share shall rank for dividend accordingly.

Any dividend or other monies payable in respect of a share may be paid by one or more of the following means:

(a) transfer to a bank or building society account specified by the distribution recipient either in writing or as the Board may otherwise decide;

(b) sending a cheque made payable to the distribution recipient by post to the distribution recipient at the distribution recipient's registered address (if the distribution recipient is a holder of the share), or (in any other case) to an address specified by the distribution recipient either in writing or as the Board may otherwise decide;

(c) sending a cheque made payable to such person by post to such person at such address as the distribution recipient has specified either in writing or as the Board may otherwise decide;

(d) by means of a relevant system in respect of shares in uncertificated form in such manner as may be consistent with the facilities and requirements of the relevant system or as the Board may otherwise decide; or

(e) by any electronic or other means as the Board may decide, to an account, or in accordance with the details specified by the distribution recipient either in writing or as the Board may otherwise decide.

5.6 ***Form and transfer of shares***

The Board may issue shares as certificated or uncertificated shares, subject to any restrictions on transfers described below:

A share held in certificated form may be transferred by an instrument of transfer in any usual form or in any other form which the Board may approve, which shall be executed by or on behalf of the transferor and, unless the share is fully paid, by or on behalf of the transferee. A share held in uncertificated form may be transferred by means of a relevant system. The transferor shall be deemed to remain the holder of the share until the transferee is entered on the register as its holder.

The Board may, in the case of shares held in certificated form, in its absolute discretion refuse to register the transfer of a share which is not fully paid provided that, where any such shares are admitted to the Official List of the UKLA or admitted to trading on AIM or ICAP Securities and Derivative Exchange (or ISDX), such discretion may not be exercised in such a way as to prevent dealings in the shares of that class from taking place on an open and proper basis.

The Board may also refuse to register a transfer of shares held in certificated form unless the instrument of transfer is:

(a) duly stamped or duly certified or otherwise shown to the satisfaction of the Board to be exempt from stamp duty, lodged at the transfer office or at such other place as the Board may appoint and (save in the case of a transfer by a person to whom no certificate was issued in respect of the shares in question) accompanied by the certificate for the shares to which it relates, and such other evidence as the Board may

reasonably require to show the right of the transferor to make the transfer and, if the instrument of transfer is executed by some other person on his behalf, the authority of that person so to do;

(b) in respect of only one class of shares; and

(c) in favour of not more than four transferees.

If the Board refuses to register a transfer of shares held in certificated form, it shall as soon as practicable and in any event within two months after the date on which the transfer was lodged with the Company send to the transferee notice of the refusal together with its reasons for the refusal.

No fee shall be charged for the registration of any instrument of transfer or other document relating to or affecting the title to any share or for making any entry in the register affecting the title to any share.

The Company shall be entitled to retain any instrument of transfer which is registered, but (except in the case of fraud) any instrument of transfer which the Board refuses to register shall be returned to the person lodging it when notice of the refusal is given.

For all purposes of these Articles relating to the registration of transfers of shares, the renunciation of the allotment of any shares by the allottee in favour of some other person shall be deemed to be a transfer and the Board shall have the same powers of refusing to give effect to such a renunciation as if it were a transfer.

If a member dies, the survivor or survivors where he was a joint holder, and his personal representatives where he was a sole holder or the only survivor of joint holders, shall be the only persons recognised by the Company as having any title to his interest; but nothing contained in these Articles shall release the estate of a deceased member from any liability in respect of any share which had been held (whether solely or jointly) by him.

5.7 ***Directors***

Unless otherwise determined by the Board, the number of directors shall be not less than two.

The directors may be paid all travelling, hotel and other expenses as they may incur in connection with their attendance at meetings of the Board or of committees of the Board or general meetings or separate meetings of the holders of any class of shares or debentures of the Company or otherwise in connection with the discharge of their duties.

The Board may provide benefits, whether by the payment of gratuities or pensions or by insurance or otherwise, for any director, employee or former employee who has held but no longer holds any office or employment with the Company or with any body corporate which is or has been a subsidiary undertaking or a predecessor in business of the Company or of any subsidiary undertaking, and for any member of his family (including a spouse and a former spouse) or any person who is or was dependent on him and may (as well before as after he ceases to hold such office or employment) contribute to any fund and pay premiums for the purchase or provision of any such benefit. The power conferred by the Act to make provision for the benefit of persons employed or formerly employed by the Company or any of its subsidiaries, in connection with the cessation or the transfer to any person of the whole or party of the undertaking of the Company or any subsidiary shall be exercised by the Board.

5.8 ***Directors' interests***

A director who to his knowledge is in any way directly or indirectly interested in a contract or arrangement or proposed contract or arrangement with the Company shall disclose the nature of his interest at a meeting of the Board.

Subject to the provisions of the Act, and provided that he has disclosed to the Board the nature and extent of any interest, a director notwithstanding his office:

(a) may be a party to, or otherwise interested in, any transaction or arrangement with the Company or in which the Company is otherwise interested;

(b) may be a director or other officer of, or employed by, or a party to any transaction or arrangement with, or otherwise interested in, any body corporate promoted by the Company or in which the Company is otherwise interested; and

(c) shall not, by reason of his office, be accountable to the Company for any benefit which he derives from any such office or employment or from any such transaction or arrangement or from any interest in any such body corporate and no such transaction or arrangement shall be liable to be avoided on the ground of any such interest or benefit.

A director may not vote (or be counted in the quorum) in respect of any resolution of the directors or committee of the directors concerning a contract, arrangement, transaction or proposal to which the Company is or is to be a party and in which he has an interest which (together with any interest of any person connected with him) is, to his knowledge, a material interest (otherwise than by his interest in Ordinary Shares or debentures or other securities of or otherwise in or through the Company). This is subject to certain exceptions including (i) where the contract, arrangements, transaction or proposal concerns general employee privileges or insurance policies for the benefit of the directors or (ii) in circumstances where a director acts in a personal capacity in the giving of a guarantee, security or indemnity for the benefit of the Company or any of its subsidiary undertakings.

Any director may act by himself or his firm in a professional capacity for the Company, other than as auditor, and he or his firm shall be entitled to remuneration for professional services as if he were not a director.

5.9 ***Borrowing powers***

The directors may exercise all the powers of the Company to borrow money and to give guarantees, hypothecate, mortgage, charge or pledge the assets, property and undertaking of the Company or any part thereof and to issue debentures and other securities whether outright or as collateral security for any debt, liability or obligation of the Company or of any third party.

5.10 ***Annual General Meetings and General Meetings***

An annual general meeting shall be held at such time and place as the Board may determine. The Board may call general meetings and, on the requisition of members pursuant to the provisions of the Act, shall forthwith convene a general meeting. If there are not sufficient directors capable of acting to call a general meeting, any director may call a general meeting. If there is no director able to act, any two members may call a general meeting for the purpose of appointing directors.

A meeting of the Company other than an annual general meeting shall be called by not less than 14 days' clear notice. An annual general meeting shall be called by not less than 21 days' clear notice. The notice shall specify the place, the day and the time of the meeting and, in the case of special business, the general nature of that business. A notice calling an annual general meeting shall specify the meeting as such and a notice for the passing of a special resolution shall specify the intention to propose the resolution as a special resolution and the terms of the resolution. Every member entitled to attend and vote is entitled to appoint one or more proxies to attend, vote and speak instead of him and that a proxy need not be a member.

The accidental omission to give notice of a meeting, or to send an instrument of proxy or invitation to appoint a proxy as provided by the Articles, to any person entitled to receive notice, or the non-receipt of notice of a meeting or instrument of proxy or invitation to appoint a proxy by such a person, shall not invalidate the proceedings at that meeting.

Every notice of meeting shall state with reasonable prominence that a member entitled to attend and vote is entitled to appoint one or more proxies to attend, vote and speak instead of him and that a proxy need not be a member.

5.11 ***Annual Report and Financial Statements***

Save as provided in the Articles, a copy of the annual accounts of the Company together with a copy of the auditors' report and the directors' report and any other documents required to accompany or to be annexed to them shall, not less than 21 clear days before the date of the general meeting at which copies of those documents are to be laid, be sent to every member and to every debenture holder of the Company and to every other person who is entitled to receive notices from the Company of general meetings.

Copies of the documents referred to in the Articles need not be sent:

(a) to a person who is not entitled to receive notices of general meetings and of whose address the Company is unaware; or

(b) to more than one of the joint holders of shares or debentures in respect of those shares or debentures,

provided that any member or debenture holder to whom a copy of such documents has not been sent shall be entitled to receive a copy free of charge on application at the registered office.

The Company may send a summary financial statement to any of the persons otherwise entitled to be sent copies of the documents referred to in the Articles instead of or in addition to those documents and, where it does so, the statement shall be delivered or sent to such person not less than 21 clear days' before the general meeting at which copies of those documents are to be laid.

5.12 ***Winding up***

If the Company is wound up, the liquidator may, with the sanction of a special resolution of the Company and any other sanction required by the Act, divide among the members in specie the whole or any part of the assets of the Company and may, for that purpose, value any assets and determine how the division shall be carried out as between the members or different classes of members. The liquidator may, with the like sanction, vest the whole or any part of the assets in trustees upon such trusts for the benefit of the members as he with the like sanction determines, but no member shall be compelled to accept any assets upon which there is a liability.

5.13 ***Untraceable shareholders***

The Company shall be entitled to sell at the best price reasonably obtainable any member's shares or the shares to which a person is entitled by virtue of transmission on death or bankruptcy or otherwise by operation of law if:

(a) for a period of twelve years, no cash dividend payable in respect of the shares has been claimed, no cheque or warrant sent by the Company through the post in a pre-paid envelope addressed to the member or to the person entitled to the shares at his address on the register or (if different) the last known address given by the member or the person so entitled to which cheques and warrants are to be sent has been paid, each attempt to make a payment in respect of the shares by means of bank transfer or other method for the payment of dividends or other monies in respect of shares has failed and no communication has been received by the Company from the member or the person so entitled (in his capacity as member or person entitled);

(b) in such period of twelve years at least three dividends (whether interim or final) have become payable on the shares;

(c) the Company has at the expiration of the said period of twelve years by advertisement in both a national newspaper and in a newspaper circulating in the area in which the address referred to in the Articles is located given notice of its intention to sell such shares; and

(d) during the period of three months following the publication of the said advertisements the Company has received no communication in respect of such share from such member or person entitled.

If at any time during or after the said period of twelve years further shares have been issued in lieu of those held at the commencement of that period or of any issued in right during that period and, since the date of issue, the requirements of the Articles have been satisfied in respect of such further shares, the Company may also sell the further shares.

To give effect to a sale pursuant to this Article, the Board may authorise any person to execute an instrument of transfer or otherwise effect the transfer of the shares to be sold. If the shares concerned are in uncertificated form, the Company may issue a written notification to the operator requiring conversion of the shares into certificated form. The purchaser shall not be bound to see to the application of the purchase monies and the title of the transferee to the shares shall not be affected by any irregularity in or invalidity of the proceedings relating to the sale. The net proceeds of sale shall belong to the Company, which shall be

obliged to account to the former member or other person previously entitled to the shares for an amount equal to the net proceeds, which shall be a debt of the Company, and shall enter the name of such former member or other person in the books of the Company as a creditor for such amount. No trust shall be created and no interest shall be payable in respect of the debt, and the Company shall not be required to account for any money earned on the net proceeds, which may be employed in the business of the Company or invested in such investments for the benefit of the Company as the Board may from time to time determine.

The provisions of the Articles applying to the Ordinary Shares will apply to the New Ordinary Shares following their creation to the same extent.

6. TAKEOVER CODE

6.1 *Mandatory bid*

The Takeover Code applies to the Company as a public limited company with its registered office in the UK. Under the Takeover Code, if an acquisition of Ordinary Shares were to increase the aggregate holding of the acquirer and its concert parties to shares carrying 30 per cent. or more of the voting rights in the Company, the acquirer and, depending on the circumstances, its concert parties, would be required (except with the consent of the Panel on Takeovers and Mergers) to make a cash offer for the outstanding Ordinary Shares in the Company at a price not less than the highest price paid for the Ordinary Shares by the acquirer or its concert parties during the previous 12 months.

This requirement would also be triggered by any acquisition of Ordinary Shares by a person holding (together with its concert parties) shares carrying between 30 and 50 per cent. of the voting rights in the Company if the effect of such acquisition were to increase that person's percentage of the total voting rights of the Company.

6.2 *Squeeze-out*

Under the Act, if an offeror were to acquire 90 per cent. of the Ordinary Shares within four months of making its offer, it could then compulsorily acquire the remaining 10 per cent. It would do so by sending a notice to outstanding Shareholders telling them that it will compulsorily acquire their shares and then, six weeks later, it would execute a transfer of the outstanding shares in its favour and pay the consideration to the Company, which would hold the consideration on trust for outstanding Shareholders.

The consideration offered to the Shareholders whose shares are compulsorily acquired under the Act must, in general, be the same as the consideration that was available under the takeover offer unless the Shareholders can show that the offer value is unfair.

6.3 *Sell-out*

The Act also gives minority Shareholders a right to be bought out in certain circumstances by an offeror who had made a takeover offer. If a takeover offer related to all the Ordinary Shares and at any time before the end of the period within which the offer could be accepted the offeror held or had agreed to acquire not less than 90 per cent. of the Ordinary Shares, any holder of shares to which the offer relates who has not accepted the offer can by a written communication to the offeror require it to acquire those shares. The offeror would be required to give any Shareholder notice of his right to be bought out within one month of that right arising.

The offeror may impose a time limit on the rights of minority Shareholders to be bought out, but that period cannot end less than three months after the end of the acceptance period. If a Shareholder exercises its rights, the offeror is bound to acquire those shares on the terms of the offer or on such other terms as may be agreed.

7. DISCLOSURE OF INTERESTS

7.1 *Directors' and other interests*

7.1.1 As at the date of this document, immediately prior to Admission, and immediately following the Placing and Admission, the interests of the Directors (including the interests of persons connected with the Directors within the meaning of section 252 of the Act) in the issued share capital of the Company (but excluding any outstanding Company Options, details of which are set out at paragraphs 7.2 and 12 of this Part VI) are as follows:

	At the date of this document			Immediately prior to Admission*		Immediately following the Placing and Admission	
Director	**Number of shares**	**Class of shares**	**Combined percentage of all issued shares**	**Number of Ordinary Shares**	**Percentage of issued Ordinary Shares**	**Number of Ordinary Shares**	**Percentage of issued Ordinary Shares**
Barry Clare[1]	148,800 404,000	Ordinary B Shares	1.5%	900,108	1.7%	900,108	1.2%
Dr Stephen Franklin	1,319,200	Ordinary	3.6%	1,319,200	2.4%	1,139,200	1.8%
John Bradshaw	—	—	—	—	—	—	—
Dr Susan Foden	—	—	—	—	—	—	—
Dr Mark Wyatt[2]	—	—	—	—	—	—	—
Dr Marc d'Abbadie[3]	—	—	—	—	—	—	—
Dr Alan Barge	—	—	—	—	—	—	—

* Includes shares issued (and subsequently re-designated and sub-divided) upon the Conversion (details of which are set out in paragraph 4.8.5 of this Part VI) and the Bonus Issue (details of which are set out in paragraph 4.8.6 of this Part VI), but excludes the Ordinary Shares to be issued in connection with the Placing.

1 Of the issued share capital of the Company set out, Barry Clare is indirectly interested in the 355,200 B Shares of the Company held by Clarat Partners LLP by virtue of being a member of Clarat Partners LLP, Barry Clare directly holds 148,800 Ordinary Shares and 48,800 B Shares as at the date of this document, and will hold 307,600 Ordinary Shares immediately prior to Admission, and 307,600 Ordinary Shares immediately following the Placing and Admission.

2 SYSCF and RSGF II are shareholders in the Company (details of their shareholdings are set out in paragraph 7.3.1 of this Part VI). Enterprise Ventures Limited manages SYSCF and RSGF II, and operates incentive schemes in connection with both SYSCF and RSGF II. Dr Mark Wyatt is an Investment Director of Enterprise Ventures Limited and participates in incentive schemes operated by that company. Accordingly, Dr Wyatt has an interest in the performance of SYSCF and RSGF II (which is, in part, influenced by the performance of the issued share capital of the Company). As at the date of this document, immediately prior to Admission, and immediately following the Placing and Admission, Dr Mark Wyatt does not and will not hold any issued share capital of the Company directly.

3 NWFB is a shareholder in the Company (details of its shareholding are set out in paragraph 7.3.1 of this Part VI). SPARK Impact Limited manages NWFB. Dr d'Abbadie is an employee of SPARK Impact Limited. He also holds a carried interest in NWFB. Accordingly, Dr d'Abbadie has an interest in the performance of NWFB (which is, in part, influenced by the performance of the issued share capital of the Company). As at the date of this document, immediately prior to Admission, and immediately following the Placing and Admission, Dr d'Abbadie does not and will not hold any issued share capital of the Company directly.

7.2 ***Outstanding Company Options and Loan Notes held by Directors***

7.2.1 As at the date of this document, the following Company Options are held by the Executive Directors:

Option Holder	Date of Grant	Number of Ordinary Shares	Exercise Price (£)	Plan under which original option granted (see paragraph 12 of this Part VI)
Barry Clare	18 August 2010	456,000	0.0088875	2008 Scheme
Barry Clare	11 January 2011	86,400	0.00875	2008 Scheme
Barry Clare	25 November 2011	272,000	0.05	Standalone Unapproved Agreement
Barry Clare	14 August 2013	224,800	0.10615	Standalone Unapproved Agreement
Dr Stephen Franklin	25 November 2011	1,015,200	0.05	2011 Plan
Dr Stephen Franklin	23 December 2013	1,940,800	0.0265375	2011 Plan
Dr Stephen Franklin	26 June 2015 (replacement for options granted on 18 August 2010)	884,000	0.008875	2011 Plan
Dr Stephen Franklin	26 June 2015 (replacement for options granted on 11 January 2011)	132,800	0.00875	2011 Plan

7.2.2 As at the date of this document, the following Company Options are held by the Non-executive Directors:

Option Holder	Date of Grant	Number of Ordinary Shares	Exercise Price (£)	Plan under which original option granted (see paragraph 12 of this Part VI)
Dr Susan Foden	25 November 2011	136,000	0.05	Standalone Unapproved Agreement
Alan Barge	1 May 2012	272,000	0.05	Standalone Unapproved Agreement

Further details about the Company Options are set out in paragraph 12 of this Part VI.

7.2.3 As at the date of this document, Clarat holds £15,000 nominal amount of 2013 Notes and has a right to the interest thereon, which will be converted into a total of 101,606 A Shares on Admission (further details of which are set out in paragraphs 10.13 to 10.14 of this Part VI). Barry Clare has an indirect interest in these 2013 Notes by virtue of being a member of Clarat. As at the date of this document, immediately prior to Admission, and immediately following the Placing and Admission, Barry Clare does not and will not hold any Loan Notes directly.

As at the date of this document, RSGF II holds £230,000 nominal amount of 2013 Notes and £99,900 nominal amount of 2014 Notes and has a right to the interest thereon, which will be converted into a total of 1,516,918 A Shares and 373,218 Ordinary Shares respectively on Admission (further details of which are set out in paragraphs 10.12 to 10.17 of this Part VI). Enterprise Ventures Limited manages RSGF II, and operates incentive schemes in connection with RSGF II. Dr Mark Wyatt, a director of the Company, is employed as an Investment Director at Enterprise Ventures Limited and through his employment participates in the incentive scheme. Accordingly, Dr Wyatt has an interest in the performance of RSGF II (which is, in part, influenced

by the performance of the Company). As at the date of this document, immediately prior to Admission, and immediately following the Placing and Admission, Dr Wyatt does not and will not hold any Loan Notes directly.

As at the date of this document, NWFB holds £544,908 nominal amount of 2013 Notes and £549,450 nominal amount of 2014 Notes and has a right to the interest thereon, which will be converted into a total of 3,590,001 A Shares and 2,050,459 Ordinary Shares on Admission (further details of which are set out in paragraphs 10.12 to 10.17 of this Part VI). SPARK Impact Limited manages NWFB. Dr d'Abbadie, a director of the Company, is employed by SPARK Impact Limited. He also holds carried interest in NWFB. Accordingly, Dr d'Abbadie has an interest in the performance of NWFB (which is, in part, influenced by the performance of the Company). As at the date of this document, immediately prior to Admission, and immediately following the Placing and Admission, Dr d'Abbadie does not and will not hold any Loan Notes directly.

7.2.4 Save as set out in paragraph 7.2.3 of this Part VI, no Director holds Loan Notes (directly or indirectly).

7.2.5 Each of the options listed in paragraphs 7.2.1 and 7.2.2 of this Part VI was originally granted under one of the option schemes adopted by Evgen or under standalone unapproved agreements entered into by Evgen. Option schemes were adopted by Evgen in July 2008 and November 2011. Following the acquisition of Evgen by the Company, those employees and directors of the Group holding outstanding options over ordinary shares in the capital of Evgen exchanged their outstanding options for Company Options. Such replacement Company Options, which are set out in the tables above in respect of Directors, will remain on the same terms as those upon which they were originally granted. Those terms are summarised in paragraph 12 of this Part VI.

7.2.6 1,506,400 of the options over Ordinary Shares held by executive Directors and 408,000 of options over Ordinary Shares held by non-executive Directors are fully vested as at the date of this document. All of the options held by executive Directors (with the exception of the option granted to Dr Franklin on 23 December 2013) and all of the options held by non-executive Directors become exercisable in full on Admission.

7.2.7 Save as disclosed in paragraphs 7.2.1 and 7.2.2 of this Part VI, none of the Directors, nor any member of their families, nor any person connected with them within the meaning of section 252 of the Act, has any interest in the issued share capital of the Company or its subsidiaries.

7.2.8 Save as disclosed in this paragraph 7.2 of this Part VI, as at the date of this document, no Director has any option over or warrant to subscribe for any shares in the Company.

7.2.9 Save for the Existing Articles, the Articles, the Deed of Variation and Termination of the Investment Agreement referred to in paragraph 10.1 of this Part VI, the NWFB Relationship Agreement referred to in paragraph 10.2 of this Part VI, the Placing Agreement referred to in paragraph 10.5 of this Part VI, the Lock-In and Orderly Market Agreements referred to in paragraph 10.6 and 10.7 of this Part VI, the 2013 Subscription Agreement and 2014 Subscription Agreement (and written consents relating to the 2013 Notes and 2014 Notes) referred to in paragraphs 10.12 to 10.17 and of this Part VI, and the service agreements and letters of appointment referred to in paragraph 9.4 of this Part VI, there are no agreements, arrangements or understandings (including compensation agreements) between any of the Directors, recent directors, shareholders or recent shareholders of the Company connected with or dependent upon Admission or the Placing.

7.2.10 Other than the Loan Notes and the Company Options, no Director or any member of their family holds or has held any financial product whose value in whole or in part is determined directly or indirectly by reference to the price of Ordinary Shares.

7.3 ***Significant Shareholders***

7.3.1 In addition to those interests disclosed at paragraphs 7.1 and 7.2 of this Part VI, the Company is aware of the following persons who, (i) at 14 October 2015 (being the latest practicable date before publication of this document), (ii) immediately prior to Admission, and (iii) immediately following completion of the Placing and Admission, have interests in voting rights over 3 per cent. or more of the issued share capital of the Company:

	At the date of this Document			Immediately prior to Admission*		Immediately following the Placing and Admission	
Shareholder	**Number of shares**	**Class of shares**	**Combined percentage of all issued shares**	**Number of Ordinary Shares**	**Percentage of issued Ordinary Shares**	**Number of Ordinary Shares**	**Percentage of issued Ordinary Shares**
RisingStars Growth Fund LP II	2,838,400 4,938,400	Ordinary A Shares	21.1%	11,950,869	22.2%	11,950,869	16.4%
North West Fund (Biomedical) LP	7,115,200	A Shares	19.3%	16,186,446	30.0%	16,186,446	22.2%
South Yorkshire Investment Fund Limited	2,838,400 765,600	Ordinary A Shares	9.8%	3,772,949	7.0%	3,772,949	5.2%
Letzone Limited	2,664,000	Ordinary	7.2%	2,664,000	4.9%	2,664,000	3.7%
Sarum Investment SICAV Plc	1,884,000	A Shares	5.1%	3,005,053	5.6%	3,005,053	4.1%
Seneca Partners Limited	1,914,400	Ordinary	5.2%	1,914,400	3.5%	3,536,022	4.9%
AXA Framlington Investment Management Limited	—	—	—	—	—	6,485,000	8.9%
Beaufort Securities Limited	—	—	—	—	—	2,457,568	3.4%

* Includes shares issued (and subsequently re-designated and sub-divided) upon the Conversion (details of which are set out in paragraph 4.8.5 of this Part VI) and the Bonus Issue (details of which are set out in paragraph 4.8.6 of this Part VI), but excludes the Ordinary Shares to be issued in connection with the Placing.

7.3.2 Save as disclosed above, the Directors are not aware of any person or persons who, directly or indirectly, have an interest in the Company which represents 3 per cent. or more of its issued share capital or voting rights who, directly or indirectly, jointly or severally, exercise or could exercise control over the Company.

7.3.3 No Director or any major shareholder has different voting rights to other holders of the share capital of the Company.

8. ADDITIONAL INFORMATION ON THE DIRECTORS

8.1 The Directors currently hold (other than in the Company) the following directorships and are partners in the following partnerships and have held the following directorships and have been partners in the following partnerships within the five years prior to the publication of this document:

Director Name	Current Directorships/ Partnerships	Former Directorships/ Partnerships
Barry Clare	Clarat Healthcare LLP Clarat Partners LLP Crescent Ops Limited Evgen Limited Famy Care Limited (India) Floback Limited HBI No. 2 Limited Healthcare Brands International Limited Helperby Therapeutics Group LimitedIngenion Medical Limited Trimb Healthcare AB (Sweden) Vantage Diagnostics Limited Walmark A.s. (Czech Republic) Xanadu Valley Limited University Hospital of South Manchester NHS Foundation Trust	Clarat Investments LLP Crescent Diagnostics Limited HBI No. 1 Limited Intermezzo Capital Limited Macsco 2011 Limited RPM Healthwatch Limited
Dr Stephen Franklin	Evgen Limited	—
John Bradshaw	Autifony SRL (Italy) Avillion LLP Avillion Financing 1 GP LP (US) Bradshaw Daniel Limited Burrowmoor Consulting Limited Evgen Limited Ixico Plc Syncona Management LLP Syncona Partners LLP	Arvia Technology Limited Autolus Limited Eight 19 Limited Labservice Limited Pneumacare Limited Vari-force Limited Women OB Limited
Dr Susan Foden	BerGenBio AS (Norway) Butterfly Conservation BTG plc Newlands Court Management Company Limited Oxford Ancestors Limited Vectura Group plc	Cascade Fund Management Limited Cellcentric Limited Cizzle Biotechnology Limited Evgen Limited Source Bioscience plc Spectrum (General Partner) Limited The Rainbow Seed Fund
Dr Mark Wyatt	Cizzle Biotechnology Limited Femeda Limited Imperial Innovations Businesses LLP Optibiotix Health Plc Optibiotix Health Limited	Ervitech Limited Mycologix Limited Smart Surgical Appliances Limited Evgen Limited
Dr Marc d'Abbadie	Dadu Investments Ltd (Mauritius) NWF4B Directors Limited Spark Impact Limited Spark NW Carry Partner LLP	Gc-Rise Pharmaceutical Co., Ltd (Cayman Islands) Technikos Capital Management LLP Technikos GP Ltd Technikos (Sc) GP Ltd
Dr Alan Barge	ASLAN Pharmaceuticals Pte. Ltd West Thorpe (2011) Limited	

8.2 Barry Clare was a director of Macsco 2011 Limited (formerly named Healthcare Brands International Limited and Healthcare Brands Limited) which was put into voluntary liquidation in 2011 in order to return exit proceeds to its shareholders.

8.3 Save as disclosed above, at the date of this document none of the Directors has:

8.3.1 any unspent convictions in relation to indictable offences (including fraudulent offences);

8.3.2 ever had any bankruptcy order made against him or entered into any individual voluntary arrangements with his creditors;

8.3.3 ever been a director of a company which has been placed in receivership, creditors' voluntary liquidation, compulsory liquidation or administration, or been subject to a voluntary arrangement or any composition or arrangement with its creditors generally or any class of its creditors, whilst he was a director of that company or within the 12 months after he ceased to be a director of that company;

8.3.4 ever been a partner in any partnership which has been placed in compulsory liquidation or administration or been the subject of a partnership voluntary arrangement whilst he was a partner in that partnership or within the 12 months after he ceased to be a partner in that partnership;

8.3.5 owned, or been a partner in a partnership which owned, any asset which, while he owned that asset, or while he was a partner or within 12 months after his ceasing to be a partner in the partnership which owned that asset, entered into receivership;

8.3.6 received any official public incrimination and/or sanction by any statutory or regulatory authority (including recognised professional bodies); or

8.3.7 been disqualified by a court from acting as a director of any company or from acting in the management or conduct of the affairs of a company.

9. DIRECTORS' SERVICE AGREEMENTS AND TERMS OF APPOINTMENT

9.1 The Group currently has two full-time employees, three part-time employees and four consultants.

9.2 Between August 2011 and April 2015 one Evgen employee, David Howat, was based in France, and during this time Evgen did not account to the French authorities for associated social security payments that may be due. Provision was made for the potential liability in the financial statements for the year ended 31 March 2015. Since 1 April 2015, David Howat has been engaged as a consultant by the Group.

9.3 The number of employees, non-executive directors and consultants on average for Evgen for each financial year and at the end of the period covered by the Historical Financial Information in Part III and at the date of this document and a breakdown of the main categories of employment are as follows:

	As at 31 March			
	2013	**2014**	**2015**	**As at the date of this document**
Administration	1	1	1	1
Executive and non-executive Directors	6	6	6	6
Consultants (not including non-executive Directors)	1	2	4	4
Total	8	9	11	11

9.4 Summary details of the service agreements and letters of appointment entered into between the Company and the Directors are set out below:

9.4.1 **Barry Clare – Executive Chairman**

Barry entered into a service agreement with the Company on 14 October 2015 to serve as Executive Chairman with effect from Admission, which is his continuous employment commencement date. Within 12 to 18 months, it is the intention of the Board to terminate the service agreement and for Barry Clare to become a Non-

executive Director of the Company. The fee to be paid in relation to such appointment shall be determined by the Remuneration Committee in advance of the appointment. His appointment is terminable on twelve months' notice by either party but in circumstances where he is being appointed as a non-executive Director of the Company, the service agreement may be terminated by the Company on one month's prior notice.

With effect from Admission, Barry's salary will be £54,000, based on a time commitment of four days per month. He is not entitled to employer pension contributions or to private medical insurance. Provision is contained in the service agreement for a discretionary bonus to be paid.

Barry's service agreement contains a non-compete restriction which applies for six months following termination of employment and other restrictions regarding non-solicitation of employees and non-interference with suppliers for twelve months following termination. It also contains protection in terms of confidential information and intellectual property.

9.4.2 **Dr Stephen Franklin – Chief Executive Officer**

Dr Franklin entered into a service agreement with the Company on 14 October 2015 to serve as Chief Executive Officer with effect from Admission. His continuous employment commencement date is 25 August 2011. His appointment is terminable on twelve months' notice by both parties.

With effect from Admission, Dr Franklin's salary will be £144,000. He is entitled to employer pension contributions of 10% of annual salary to a personal pension scheme and flexibility is built into the service agreement to allow Dr Franklin to elect for an increase in pension contributions in return for an equivalent salary reduction. Dr Franklin is entitled to private medical insurance for himself and his family.

Dr Franklin will be entitled to an annual bonus of up to but not exceeding 50% of salary based on Company and personal objectives. It is intended that the bonus earned will normally be paid in a combination of cash and deferred Shares at the discretion of the Remuneration Committee. This may be revised if there is an equivalent increase in salary.

Dr Franklin's service agreement contains a non-compete restriction which applies for six months following termination of employment and other restrictions regarding non-solicitation of employees and non-interference with suppliers for twelve months following termination. It also contains protection in terms of confidential information and intellectual property.

9.4.3 **John Bradshaw – Finance Director and Company Secretary**

John entered into a service agreement with the Company on 14 October 2015 to serve as Finance Director and Company Secretary with effect from Admission, which is his continuous employment commencement date. His appointment is terminable on twelve months' notice by both parties.

With effect from Admission, John's salary will be £36,000, based on a time commitment of three days per month. He is not entitled to employer pension contributions or private medical insurance.

John will be entitled to an annual bonus of up to but not exceeding 50% of salary based on Company and personal objectives. It is intended that the bonus earned will normally be paid in a combination of cash and deferred Shares at the discretion of the Remuneration Committee. This may be revised if there is an equivalent increase in salary.

John's service agreement contains a non-compete restriction which applies for six months following termination of employment and other restrictions regarding non-solicitation of employees and non-interference with suppliers for twelve months following termination. It also contains protection in terms of confidential information and intellectual property.

9.4.4 **Dr Susan Foden**

Dr Foden entered into a letter of appointment with the Company on 14 October 2015, which takes effect on Admission. The appointment is terminable by either side giving one month's notice. Dr Foden's annual fee will be £26,500.

9.4.5 **Dr Alan Barge**

Dr Barge entered into a letter of appointment with the Company on 14 October 2015, which takes effect on Admission. The appointment is terminable by either side giving one month's notice. Dr Barge's annual fee will be £22,500.

9.4.6 **Dr Mark Wyatt**

Dr Wyatt entered into a letter of appointment with the Company on 14 October 2015, which takes effect on Admission. The appointment is terminable by either side giving one month's notice. Dr Wyatt's annual fee will be £22,500, which sum will be paid to Enterprise Ventures Limited.

9.4.7 **Dr Marc d'Abbadie**

Dr d'Abbadie entered into a letter of appointment with the Company on 14 October 2015, which takes effect on Admission. The appointment is terminable by either side giving one month's notice. Dr d'Abbadie's annual fee will be £26,500, and will be payable to SPARK Impact Limited, or such other person as SPARK Impact Limited may direct from time to time.

9.5 The Chairman and Non-executive Directors are entitled to be reimbursed for their expenses.

9.6 Save as set out above, there are no contracts providing for benefits upon termination of employment of any Director.

10. MATERIAL CONTRACTS

The following contracts, not being contracts entered into in the ordinary course of business, have been entered into by the Group within the two years immediately preceding the date of this document and are, or may be, material:

10.1 ***Deed of Adherence and Variation***

On 5 December 2014, the Company entered into a deed of adherence and variation with Evgen and the other parties to the Investment Agreement pursuant to which the Company agreed to assume, from completion of the Share for Share Exchange, the outstanding rights, interests, responsibilities, liabilities, undertakings and obligations of Evgen under the Investment Agreement as if any reference therein to shares in Evgen was a reference to the equivalent class of shares in the Company, and as if any reference therein to Evgen was a reference to the Company. The Investment Agreement (as adhered to and varied by this agreement) regulates the operation and management of the Company and the relationship between the Company's shareholders. The parties agreed to terminate the Investment Agreement (as adhered to and varied by this agreement) immediately prior to Admission.

10.2 ***NWFB Relationship Agreement***

On 14 October 2015, the Company and NWFB entered into a relationship agreement (the "**NWFB Relationship Agreement**") pursuant to which the Company gave certain acknowledgements, undertakings and confirmations to NWFB regarding, amongst other things, the maintenance of its records, the provision of information, its compliance with applicable laws, regulation and guidance, its approach to capital purchases, and its co-operation in ensuring that NWFB complies with its obligations to the European Investment Bank and the European Regional Development Fund.

The NWFB Relationship Agreement provides that if:

10.2.1 the investment in the Company by NWFB is deemed to be or becomes ineligible under the investment objectives and policies of NWFB (as the same may be varied from time to time at the discretion of, in particular, the European Investment Bank, the European Regional Development Fund and NWFB);

10.2.2 there has been a breach of those objectives and policies; or

10.2.3 the European Investment Bank, the European Regional Development Fund, NWFB or other body connected with NWFB are obliged to pay back monies which they made available to NWFB,

and NWFB so demands, then the Company must repay NWFB in such a manner and at such time as NWFB may determine, all ineligible monies which have been made available to the Company by NWFB.

10.3 ***Share for Share Exchange Agreement***

On 5 December 2014, an agreement was entered into between the Company and the shareholders of Evgen at that time (the "**Share for Share Exchange Agreement**") whereby each such shareholder in Evgen agreed to exchange their shares in Evgen for a corresponding number of shares of the same class in the Company (the "**Share for Share Exchange**").

10.4 ***Options Exchange Agreements***

On 25 June 2015, the Company and holders of Evgen Options entered into documentation whereby the holders of Evgen Options over ordinary shares in Evgen surrendered their Evgen Options in exchange for the Company granting them replacement Company Options over Ordinary Shares. All replacement Company Options were granted on the same terms as the existing Evgen Options. Further details on the Company Options are set out in paragraph 12 of this Part VI.

10.5 ***Placing Agreement***

On 14 October 2015, the Company, each of the Directors, David Howat and Northland Capital entered into the Placing Agreement (the "**Placing Agreement**") pursuant to which, subject to certain conditions, Northland Capital has agreed to use its reasonable endeavours to procure subscribers for the New Ordinary Shares at the Placing Price. The Placing Agreement contains customary indemnities and warranties from the Company and warranties from the Directors and David Howat in favour of Northland Capital, together with provisions which enable Northland Capital to terminate the Placing Agreement in certain circumstances, including circumstances where any of the warranties are found to be untrue or inaccurate or misleading in any material respect. For its services in connection with the Placing and Admission, the Company has agreed to pay to Northland Capital a corporate finance fee and a commission equal to the aggregate of (i) 5 per cent. of the aggregate value at the Placing Price of the number of Placing Shares placed by Northland Capital and (ii) 0.5 per cent of the aggregate value at the Placing Price of the number of Placing Shares placed by the Company or any third party (including but not limited to Acceleris) and to issue Warrants to Northland Capital pursuant to which Northland Capital will have the right to subscribe for 728,709 Ordinary Shares, constituting 1 per cent. of the enlarged issued share capital of the Company immediately following Admission, at a price of 37p per Ordinary Share, being the Placing Price.

Further details on the Warrants are set out in paragraph 10.8 of this Part VI.

Pursuant to the Placing Agreement, the Directors and David Howat have undertaken, subject to certain limited exceptions, not to dispose of any of the Ordinary Shares which they will hold following Admission for a period until 12 months from Admission. In addition, orderly marketing arrangements apply for a further period of 12 months following the expiry of the lock-in period referred to above whereby the Directors and David Howat have undertaken to sell Ordinary Shares through Northland Capital (or such other reputable broker appointed by the Company from time to time) or in the event that Northland Capital (or such other reputable broker appointed by the Company) cannot place the relevant number of Ordinary Shares at the requested price, through a third party broker at a higher price and on terms no less favourable than those offered by Northland Capital (or such other reputable broker appointed by the Company).

10.6 ***Hard Lock-In and Orderly Market Agreements***

In addition to the lock-in and orderly market provisions that apply to the Directors and David Howat under the Placing Agreement (details of which are set out in paragraph 10.5 of this Part VI), pursuant to lock-in and orderly market agreements dated 14 October 2015, (the "**Hard Lock-in and Orderly Market Agreements**"):

10.6.1 Certain Shareholders, including NWFB, RSGF II, SYSCF and Sarum Capital, have agreed with the Company and Northland Capital, subject to certain limited exceptions, not to dispose of, in aggregate, 39,508,742 Ordinary Shares owned by them for a period of 12 months from Admission;

10.6.2 Certain Shareholders have agreed with the Company and Northland Capital not to dispose of, in aggregate, 7,176,800 Ordinary Shares owned by them for a period of 12 months from Admission, subject to certain limited exceptions, including should the Company's volume weighted average share price exceed 200% of the Placing Price for a period of 20 consecutive business days during the 12 months from Admission; and

10.6.3 The Shareholders who are a party to the Hard Lock-in and Orderly Marketing Agreements as referred to in paragraphs 10.6.1 and 10.6.2 of this Part VI have also agreed with the Company and Northland Capital, subject to certain limited exceptions, to dispose of Ordinary Shares owned by them, for a period of 12 from months from the end of the period referred to in paragraphs 10.6.1 and 10.6.2 of this Part VI, only through Northland Capital (or such other reputable broker appointed by the Company from time to time) or in the event that Northland Capital (or such other reputable broker appointed by the Company) cannot place the relevant number of Ordinary Shares at the requested price, through a third party broker at a higher price and on terms no less favourable than those offered by Northland Capital (or such other reputable broker appointed by the Company),

in each case, in order to ensure an orderly market for the issued share capital of the Company.

10.7 ***Soft Lock-in and Orderly Market Agreements***

In addition to the lock-in and orderly market provisions that apply to the Directors and David Howat pursuant to the Placing Agreement (details of which are set out in paragraph 10.5 of this Part VI) and to certain Shareholders, including NWFB, RSGF II, SYSCF and Sarum Capital, pursuant to the Hard Lock-in and Orderly Market Agreements (details of which are set out in paragraph 10.6 of this Part VI), pursuant to lock-in and orderly market agreements dated 14 October 2015, (the "**Soft Lock-in and Orderly Market Agreements**"), certain other existing Shareholders have agreed with the Company and Northland Capital, subject to certain limited exceptions, to dispose of, in aggregate, 3,443,733 Ordinary Shares owned by them, for a period of 6 to 12 months from Admission, only through Northland Capital (or such other reputable broker appointed by the Company from time to time) or in the event that Northland Capital (or such other reputable broker appointed by the Company) cannot place the relevant number of Ordinary Shares at the requested price, through a third party broker at a higher price and on terms no less favourable than those offered by Northland Capital (or such other reputable broker appointed by the Company), in order to ensure an orderly market for the issued share capital of the Company.

10.8 ***Warrant Instrument***

On 14 October 2015, the Company entered into a warrant instrument (the "**Warrant Instrument**") pursuant to which the Company has constituted warrants to subscribe for Ordinary Shares (the "**Warrants**"). Pursuant to the terms of the Placing Agreement (details of which are at paragraph 10.5 of this Part VI), the Company shall issue to 728,709 Warrants to Northland Capital. Pursuant to the terms of Acceleris Engagement Letter (details of which are set out paragraph 10.18 of the Part VI), the Company shall issue 728,709 Warrants to Acceleris. Each Warrant entitles the holder to subscribe for one Ordinary Share at £0.37 per Ordinary Share at any time in the period from the date of Admission to and including the fifth anniversary of Admission. If at any time while the Warrants are exercisable, an offer is made to the holders of all the Ordinary Shares (or all such holders other than the offeror and/or persons acting in concert with the offeror) to acquire the whole or any part of the equity share capital of the Company and the Company becomes aware that as a result of such an offer the right to cast a majority of the votes which may ordinarily be cast on a poll at a general meeting of the Company ("**Control**") has or will become vested in the offeror and/or such persons as aforesaid, the Company shall give notice to the holders of Warrants within 7 days of it becoming so aware, and any holder of Warrants shall either be entitled at any time within 20 days thereafter to exercise their Warrants or to require the Company, so far as it is able, to procure that a like offer or invitation for any Warrants held by such holder is

made as if such Warrants had been exercised in full and as if the Ordinary Shares issued pursuant to such exercise had been issued immediately prior to the record date for such offer or invitation in each case subject to remittance to the Company of the aggregate subscription price due on the exercise of such Warrants). Any Warrants which are not exercised or in respect of which a like offer or invitation is not accepted within such 20 day period, shall lapse and shall not thereafter be capable of being exercised.

10.9 ***Nomad and Broker Agreement***

On 14 October 2015, the Company and Northland Capital entered into a nomad and broker agreement pursuant to which the Company has, conditional on Admission, appointed Northland Capital to act as nominated adviser and corporate broker to the Company for the purposes of the AIM Rules. The Company has agreed to pay Northland Capital a fee of £45,000 per annum for its services as nominated adviser and broker under the agreement, together with all reasonable out of pocket expenses and VAT. The agreement contains certain indemnities and undertakings given by the Company. The agreement continues for an initial period of twelve months from Admission and thereafter may be terminated by either party giving the other three month's written notice.

10.10 ***Registrars Agreement***

On 14 October 2015, the Company and the Registrar entered into a registrar agreement under which the Registrar has agreed to provide services connected with the maintenance of the Company's register, including where shares are issued or transferred and dividends declared. The agreement is for an initial period of 12 months, and thereafter will continue until terminated by either party giving not less than 3 months' notice.

10.11 ***Patent and Know-How Licence Agreement***

Evgen entered into a patent and know-how licence agreement with PharmAgra and Lalilab Inc. dated 21 October 2013 (superseding an earlier agreement) (the "**Patent and Know-How Licence**"). The Patent and Know-How Licence grants Evgen the exclusive right to exploit Sulforaphane stabilisation technology for pharmaceutical purposes.

PharmAgra and Lalilab Inc. have an exclusive back-licence to develop and exploit the technology in the excluded fields of topical applications. Evgen is prohibited from developing and selling any stabilised Sulforaphane products that are non-topically applied treatments for non-cancerous/pre-cancerous conditions specifically associated with the skin, eyes, ears or nose in any format.

10.12 ***2013 Subscription Agreement***

On 2 July 2013, Evgen, Stephen Franklin, NWFB, RSGF II, and Clarat entered into a subscription agreement (the "**2013 Subscription Agreement**") pursuant to which NWFB, RSGF II and Clarat subscribed for 2013 Notes with an aggregate nominal value of £85,000. The 2013 Subscription Agreement was subsequently amended by a deed of variation dated 30 October 2013 among the same parties. The 2013 Subscription Agreement provided for Evgen to issue, at any time within 9 months of the issue of the initial £85,000 of 2013 Notes to NWFB, RSGF II and Clarat, an additional £915,000 of 2013 Notes. A total of £1,000,000 of 2013 Notes were issued under the 2013 Subscription Agreement (as amended). Evgen and Stephen Franklin gave certain specific warranties to NWFB which NWFB required to satisfy its funding restrictions.

10.13 ***2013 Loan Note Instrument***

On 30 October 2013, Evgen entered into an amended and restated unsecured convertible loan note instrument (the "**2013 Loan Note Instrument**") which amended and restated the unsecured convertible loan note instrument entered into by Evgen on 2 July 2013. Evgen has issued £1,000,000 in nominal value of unsecured convertible loan notes pursuant to the 2013 Loan Note Instrument (the **"2013 Notes**").

The 2013 Notes are repayable bi-annually on the basis of 1/1000 of the principal outstanding (plus accrued but unpaid interest) being paid each year until 30 April 2017 when all remaining outstanding 2013 Notes will be repaid with all unpaid interest. Interest accrues daily on the 2013 Notes at a rate of 11 per cent. per annum, which is rolled up and either paid on the relevant repayment date, or converted into shares in Evgen on the occurrence of a conversion event.

As at the date of this document, the principal outstanding under the 2013 Notes in issue is £998,308. All outstanding 2013 Notes will automatically convert into A Shares (which will subsequently be re-designated as Ordinary Shares) at a price of £0.185 per share, being a 50 per cent. discount to the Placing Price conditional on Admission.

10.14 ***2013 Loan Note Deed of Novation***

On 25 June 2015, a deed of novation was entered into between the Company and Evgen (the "**2013 Loan Note Deed of Novation**") pursuant to which the Company agreed to assume the outstanding rights, interests, liabilities and obligations of Evgen under the 2013 Loan Note Instrument as if any reference therein to shares in Evgen was a reference to the equivalent class of shares in the Company, and as if any reference therein to Evgen was a reference to the Company. Written consent for such novation was obtained from the requisite majority of holders of 2013 Notes.

The Placing will constitute a "Qualified Fund Raising" and Admission will constitute a "Qualified Listing" (each as defined under the 2013 Loan Note Instrument). Consequently, all outstanding 2013 Notes, together with all accrued but unpaid interest on them, will automatically convert into fully paid A Shares in the Company at a price of £0.185 per share being a 50 per cent. discount to the Placing Price immediately prior to Admission.

10.15 ***2014 Subscription Agreement***

On 3 November 2014, Evgen, Stephen Franklin, RSGF II, Walker Crips and NWFB entered into a subscription agreement pursuant to which RSGF II, Walker Crips and NWFB subscribed for 2014 Notes with an aggregate nominal value of £750,000. Evgen and Stephen Franklin gave customary warranties to the Walker Crips (but did not extend those general warranties to NWFB, RSGF II or any other party). Evgen and Stephen Franklin gave the same warranties to NWFB as they did in the 2013 Subscription Agreement.

10.16 ***2014 Loan Note Instrument***

On 3 November 2014, Evgen entered into an unsecured convertible loan note instrument (the "**2014 Loan Note Instrument**"). Evgen has issued £750,000 in nominal value of unsecured convertible loan notes under the 2014 Loan Note Instrument (the "**2014 Notes**").

The 2014 Notes are repayable bi-annually on the basis of 1/1000 of the principal outstanding (plus accrued but unpaid interest) being paid each year until 2 January 2017 when all remaining outstanding 2014 Notes will be repaid with all unpaid interest. Interest accrues daily on the 2014 Notes at a rate of 11 per cent. per annum, which is rolled up and either paid on the relevant repayment date, or converted into shares in Evgen on the occurrence of a conversion event.

As at the date of this document, the principal outstanding under the 2014 Notes in issue was £749,250. The requisite majority of holders of 2014 Notes have given their consent to the conversion of all outstanding 2014 Notes into Ordinary Shares at a price of £0.296 per share, being a 20 per cent. discount to the Placing Price conditional on Admission.

10.17 ***2014 Loan Note Deed of Novation***

On 25 June 2015, a deed of novation was entered into between the Company and Evgen (the "**2014 Loan Note Deed of Novation**") pursuant to which the Company agreed to assume the outstanding rights, interests, liabilities and obligations of Evgen under the 2014 Loan Note Instrument as if any reference therein to shares in Evgen was a reference to the equivalent class of shares in the Company, and as if any reference therein to Evgen was a reference to the Company. Written consent for such novation was obtained from the requisite majority of holders of 2014 Notes.

Admission will constitute a "Listing" (as defined under the 2014 Loan Note Instrument). The requisite majority of the holders of the 2014 Notes have given their consent to the conversion of the outstanding 2014 Notes, together with all accrued but unpaid interest on them, into fully paid Ordinary Shares at a price of £0.296 per share, being a 20 per cent. discount to the Placing Price immediately prior to Admission.

10.18 ***Engagement letter with Acceleris***

On 16 July 2015, Evgen and Acceleris entered into an engagement letter pursuant to which Acceleris agreed to provide corporate finance advice to the Company and Evgen, including assistance in raising new finance by way of an issue of Ordinary Shares in the Pre-IPO

Round and the Placing. Evgen has agreed for itself and on behalf of the Company to pay Acceleris (i) a corporate finance fee of £15,000, (ii) a success fee of £35,000 conditional on Admission, (iii) a commission of 0.5 per cent. on all monies raised in the Pre-IPO Round and the Placing from whatever sources, (iv) a commission of 6 per cent. on all monies raised on monies raised in the Pre-IPO Round from placees identified by Acceleris, and (v) a commission of 4 per cent. on all monies raised in the Placing from placees identified by Acceleris. In addition, the Company has agreed to issue 728,709 Warrants to Acceleris pursuant to which Acceleris will have the right to subscribe for Ordinary Shares, constituting 1 per cent. of the enlarged issued share capital of the Company immediately following Admission at a price of £0.37 per Ordinary Share, being the Placing Price. The Company has also agreed to retain Acceleris to provide corporate finance advice as part of a one-year rolling contract at an annual retainer of £20,000. In the event that the Company terminates the appointment of Acceleris in the initial three year period following Admission, the Company must pay Acceleris the sum of £60,000, less any amount of the annual retainer already paid.

10.19 ***Pre-IPO Round***

On 26 August 2015, 9,569 ordinary shares of £2.00 each were allotted to subscribers procured by Acceleris at £209 per share pursuant to the Pre-IPO Round. Subscriptions were accepted on the basis of application forms. Subscribers who were not already Shareholders executed a personalised deed of adherence with the Company in which they undertook to comply with the relevant provisions of the Investment Agreement.

11. INTELLECTUAL PROPERTY RIGHTS

11.1 Pursuant to the Patent and Know-How Licence (details of which are set out in paragraph 10.11 of this Part VI), the Group has the exclusive right to exploit the following 18 patents for pharmaceutical purposes in respect of Sulforaphane stabilisation technology. The patents are registered in the name of PharmAgra but the patents can be assigned to the Group once 50 patients have been recruited into a clinical trial. Three of these patents have been granted and applications are pending in respect of the remaining fifteen.

Type	Country	Application No.	Registration No.	Application Date	Status	Expiry Date
Patent	Australia	AU2008209543	AU2008209543	23/1/2008	Granted	23/1/2028
Patent	Canada	CA2,672,971	CA2,672,971	23/1/2008	Granted	23/1/2028
Patent	USA	US12/009,874	US7,879,822	23/1/2008	Granted	23/1/2028 293 days
Patent	European Divisional	EP14166888.9	N/A	23/1/2008	Pending	23/1/2028
Patent	Hong Kong	14113030.9	N/A	23/1/2008	Pending	23/1/2028
Patent	Japanese Divisional	2013—210752	N/A	23/1/2008	Pending	23/1/2028
Patent	Australia	AU2013269340	N/A	31/5/2013	Pending	31/5/2033
Patent	Brazil	BR1120140 298416	N/A	31/5/2013	Pending	31/5/2033
Patent	Canda	2,875,063	N/A	31/5/2013	Pending	31/5/2033
Patent	China	CN201380040262	N/A	31/5/2013	Pending	31/5/2033
Patent	Europe	EP13726846.2	N/A	31/5/2013	Pending	31/5/2033
Patent	India	10764/DELNP/ 2014	N/A	31/5/2013	Pending	31/5/2033
Patent	Japan	2015-514596	N/A	31/5/2013	Pending	31/5/2033
Patent	USA	US14/404,773	N/A	31/5/2013	Pending	31/5/2033
Patent	China	CN20138004 02677	N/A	31/5/2013	Pending	31/5/2033
Patent	Europe	EP13730628.8	N/A	31/5/2013	Pending	31/5/2033
Patent	Japan	2015-514595	N/A	31/5/2013	Pending	31/5/2033
Patent	USA	US14/404,781	N/A	31/5/2013	Pending	31/5/2033

11.2 The Group has entered into an exclusive option with Consejo Superior de Investigaciones Scientificas (CSIS) and Universidad de Sevilla to take an exclusive licence to develop novel sulforaphane analogues using the other parties' technology. On 1 September 2015, Evgen issued its notice to convert the option to a worldwide exclusive licence agreement in-line with the headline terms as detailed in the option agreement. The Directors expect to execute the

licence agreement prior to 1 December 2015. The granted patent and pending patent applications relating to the technology are registered in the name of CSIS and Universidad de Sevilla.

Type	Country	Application No.	Registration No.	Application Date	Status	Expiry Date
Patent	Spain	P201230356	201.230.356	9/3/2012	Granted	9/3/2032
Patent	Australia	AU2013229355	N/A	6/3/2013	Pending	6/3/2033
Patent	Canada	2,866,740		6/3/2013	Pending	6/3/2033
Patent	China	201380013103.5		6/3/2013	Pending	6/3/2033
Patent	Europe	EP13757087.5		6/3/2013	Pending	6/3/2033
Patent	Japan	2014-560416		6/3/2013	Pending	6/3/2033
Patent	USA	14/383,780		6/3/2013	Pending	6/3/2033

11.3 Evgen owns the registered trademarks listed below:

Trademark	Territory	Application No.	Class(es)	Filing Date
Evgen	United Kingdom	2496447	5/36/42	1 September 2008
Sulforadex®	United Kingdom	2538957	5	12 February 2010
Sulforadex®	European Community	10289528	5	26 September 2011
Sulforadex®	United States	85432458	5	26 September 2011

12. EMPLOYEE SHARE SCHEMES AND INCENTIVE PLANS

12.1 ***Introduction***

Evgen adopted the following share plans:

(a) the Evgen 2008 Share Option Scheme which was established by resolution of the board of directors of Evgen passed on 24 July 2008 and approved by the shareholders of Evgen by ordinary resolution passed on 24 July 2008 (the "**2008 Scheme**"); and

(b) the Evgen Limited Enterprise Management Incentive (EMI) Share Option Plan dated 25 November 2011 (the "**2011 Plan**").

In addition to the options granted under the 2008 Scheme and the 2011 Plan, options were also granted to employees and directors of Evgen pursuant to standalone unapproved share option agreements entered into by Evgen ("**Standalone Unapproved Agreements**").

The share options granted by Evgen pursuant to all such arrangements referred to above are together referred to herein as the "**Evgen Options**".

Following the Share for Share Exchange, all optionholders holding Evgen Options exchanged their Evgen Options (the "**Option Exchange Agreement**") for the grant of replacement options over ordinary shares of £2 in the capital of the Company (the "**Company Options**"). All Company Options are on the same terms as the corresponding Evgen Options. References in this paragraph 12 of this Part VI to Evgen Options shall be read as references to the corresponding exchanged Company Options.

Following the Sub-division referred to in paragraph 4.8.2 of this Part VI, the terms of the Company Options were adjusted (in accordance with the variation of share capital provisions of each scheme as set out in this paragraph 12) so that every Company Option over one ordinary share of £2 in the capital of the Company in existence prior to the Sub-division was deemed to be an option over 800 Ordinary Shares and the price per Ordinary Share payable upon the exercise of an option was deemed to be one 1/800th of the exercise price of such Company Option.

The Company intends to adopt the Evgen Pharma Long Term Incentive Plan (the "**LTIP**") and the Evgen Pharma Deferred Bonus Plan (the "**DBP**"), conditional upon Admission, to incentivise Directors and employees of the Group after Admission. The rules of the LTIP provide that, in any period of 10 calendar years, not more than 10 per cent. of the Company's issued ordinary share capital may be issued under the LTIP and under any other employees' share scheme operated by the Company, including the DBP. Ordinary Shares issued or to be issued pursuant to awards or options granted on or before Admission or the LTIP IPO Awards (as defined in paragraph 12.5.4 below) will not count towards these limits.

It is intended that the operation of the Company's share plans will be supervised by the Remuneration Committee. References to the Board in this paragraph 12 should be read as referring to the Remuneration Committee as appropriate.

12.2 ***2008 Option Scheme***

12.2.1 ***Outline***

The 2008 Scheme provides for the grant of unapproved and tax favoured Enterprise Management Incentive Scheme ("**EMI**") options granted under the provisions of schedule 5 to the Income Tax (Earnings and Pensions) Act 2003 ("**Schedule 5 ITEPA**") to selected employees and directors of Evgen to acquire Ordinary Shares ("**2008 Scheme Options**"). Any EMI options granted under the 2008 Scheme have lapsed or been surrendered.

No further options were granted under the 2008 Scheme following the Company's adoption of the 2011 EMI Plan. The 2008 Scheme closed to the grant of new options following the Option Exchange Agreement. Pursuant to the Option Exchange Agreement, employees and directors holding 2008 Scheme Options exchanged their 2008 Scheme Options for options over ordinary shares of £2 in the capital of the Company on the same terms as their 2008 Scheme Options over Evgen ordinary shares.

12.2.2 ***Outstanding Options***

As at the date of this document, there are 2008 Scheme Options over 1,153,600 Ordinary Shares.

12.2.3 ***Eligibility***

2008 Scheme Options can be granted to any director or *bona fide* employee of the Company and any subsidiary of the Company. EMI options can only be granted to eligible employees pursuant to Schedule 5 ITEPA, namely those whose committed time (for the purposes of Schedule 5 ITEPA) amounts to at least 25 hours a week or, if less, 75 per cent. of his working time and has no material interest (for the purposes of Schedule 5 ITEPA) in the Company.

12.2.4 ***Grant of Options***

2008 Scheme Options can be granted at any time until 24 July 2018, being the tenth anniversary of date of adoption of the rules of the 2008 Scheme unless the Company is restricted from granting 2008 Scheme Options by any statute, order or regulation.

12.2.5 ***Exercise Price***

The price per Ordinary Share payable ranges from £0.05 to £0.00875.

12.2.6 ***Individual limits on participation***

There are no individual limits on participation in the 2008 Scheme, subject to the limit set out in Schedule 5 ITEPA at the date of grant which restricts the grant of EMI options (see paragraph 12.2.7 of this Part VI).

12.2.7 ***EMI Options Limits***

The applicable limits set out in Schedule 5 ITEPA apply to any EMI options awarded under the 2008 Scheme, namely that the Company cannot grant EMI options over Ordinary Shares with a total market value of more than £3 million (such value being measured at the date of grant of the options) and that each individual cannot be granted EMI options with a total market value of more than £250,000 (again, measured at the date of grant of the relevant option). This applies to all EMI options granted over Ordinary Shares, whether granted under the 2008 Scheme, the 2011 Plan or otherwise.

12.2.8 ***Sourcing the Option Shares***

The Company must issue or otherwise transfer the Ordinary Shares acquired by optionholders within 30 days of exercise of their 2008 Scheme Options.

12.2.9 ***Exercise and lapse of options***

The 2008 Scheme Options all provide that they are all fully vested on an AIM admission, to the extent that such options were not already vested.

All 2008 Scheme Options therefore become exercisable following Admission (to the extent that they were not already exercisable). The 2008 Scheme Options lapse on the earliest of:

- the end of the performance period if the performance target is not satisfied;
- six months after the date of cessation if an employee or director ceases to hold office or employment by reason of injury, ill-health or disability, the fact that the office or employment relates to a business or part of a business which is transferred to a third party or the fact that the Company the optionholder is an office holder or employee of is no longer a member of the Company's group;
- at the end of a period which the Board determines on cessation of employment for any other reason;
- 12 months after death of an optionholder;
- six months after a change of control (see paragraph 12.2.12 of this Part VI);
- a person ceasing to be entitled or bound to acquire shares under Chapter 3 of Part 28 of the Act (see paragraph 12.2.12 of this Part VI);
- commencement of a voluntary winding-up of the Company (see paragraph 12.2.11 of this Part VI);
- one month after notification of a proposed demerger of the Company (see paragraph 12.2.11 of this Part VI); and
- three months after a court sanctions a compromise or arrangement for the purposes of a scheme of reconstruction pursuant to section 899 of the Act (see paragraph 12.2.11 of this Part VI).

12.2.10 ***Internal reconstruction***

Optionholders may be invited, before their 2008 Scheme Options lapse, to exchange their 2008 Scheme Options for options in the acquiring company which are in the opinion of the Board substantially equivalent in value to the value of the 2008 Scheme Option in question and on terms approved by the Board in the event of a demerger, reorganisation, reconstruction or amalgamation where substantially all of the existing shareholders of the Company immediately after the change of control own more than 50 per cent. of the issued ordinary share capital of the acquiring company.

12.2.11 ***Demerger, reconstruction or winding-up of the Company***

If the Company's shareholders are notified of a proposed demerger of the Company or any subsidiary, optionholders may exercise their 2008 Scheme Options within one month (or such longer period as the Board may specify and notify to optionholders) and 2008 Scheme Options shall lapse at the end of that period.

If a court sanctions a compromise or arrangement for the purposes of, or in connection with, a scheme for the reconstruction of the Company or its amalgamation pursuant to section 899 of the Act, the 2008 Scheme Options are exercisable within three months commencing on the date on which the compromise or arrangement becomes effective (or, if the Board so determines, the earlier date when the court sanctions the compromise or arrangement). The 2008 Scheme Options lapse at the end of the three month period. The Board may permit optionholders to exercise their 2008 Scheme Options conditional upon the court sanctioning such compromise or arrangement, but before the compromise or arrangement becomes effective.

If the Company's shareholders are notified of a resolution for the voluntary winding up of the Company, the 2008 Scheme Options may be exercised at any time before the winding-up commences, or within such other period as the Board notifies to optionholders. The 2008 Scheme Options lapse upon the commencement of the winding-up.

12.2.12 ***Takeover of the Company***

2008 Scheme Options may be exercised within six months of a change of control and shall lapse at the end of that period. For the purposes of the 2008 Scheme, a change of control is the Company coming under the control of another person or persons, all of whom are otherwise unconnected with the Company and its group, by way of either

(i) a general offer to acquire the whole of the ordinary share capital of the Company, (ii) a general offer to acquire all of the shares of the same class as the option shares, namely the Ordinary Shares or (iii) a compromise or arrangement sanctioned by the court pursuant to section 899 of the Act.

If any person becomes entitled or bound to acquire shares in the Company under Chapter 3 of Part 28 of the Act, the 2008 Scheme Options may be exercised at any time when that person remains so entitled or bound and shall lapse when that person is no longer so entitled or bound.

12.2.13 ***National Insurance Contributions (''NICs'')***

Each 2008 Scheme Option agreement specifies that the optionholder's employer may recover from that optionholder (in such manner as the Board may determine and notify before the option is exercised) the whole or part of any employer's NICs payable in connection with the option. The Company may request, before any 2008 Scheme Option is exercised, that the optionholder enters into an election under paragraph 3B of Schedule 1 to the Social Security Contributions and Benefits Act 992 to transfer the whole or part of any employer's NICs.

Each optionholder has granted an indemnity to the Company and the optionholder's employer, if different, in respect of any option tax liability, namely any income tax, employee's NICs and employer's NICs (if requested by the Company – see above) payable by the Company (or any other member of the Group). To the extent that the amount of such tax liability has not been withheld from the optionholder's remuneration or payment otherwise made to the Company by the optionholder (or agreed to be made within 14 days of notification of the amount of the liability), the Company may sell as agent a sufficient number of Ordinary Shares acquired pursuant to the 2008 Scheme Option to procure payment of the liability (after deduction of all fees, commissions and expenses incurred in relation to such sale).

12.2.14 ***Variation of Share Capital***

The Board shall adjust the aggregate number of shares subject to option and exercise price for each share under option as they consider appropriate in the event of any alteration of the ordinary share capital of the Company by way of capitalisation or rights issue, sub-division, consolidation or reduction or any other variation in the share capital of the Company. Any adjustment in the case of a sub-division, consolidation or capitalisation issue must be confirmed by such firm of professional advisers as the Board may specify to be, in the opinion of those advisers, fair and reasonable.

12.2.15 ***Amendment of the Share Scheme***

The Board may alter or add to the provisions of the 2008 Scheme at any time provided that no alteration or addition may be made to the advantage of existing or new optionholders or to the alteration clause without the prior approval by ordinary resolution of the shareholders of the Company. Any amendments which are, in the opinion of the Board, minor to take account of any change in legislation or to obtain or maintain favourable tax, exchange control or regulatory treatment for existing or new optionholders or any member of the Company's group do not require such prior approval.

12.3 ***2011 Plan***

12.3.1 ***Outline***

The 2011 Plan provides for the grant of unapproved and tax favoured EMI options granted under the provisions of Schedule 5 ITEPA to selected employees of the Company to acquire Ordinary Shares (''**2011 Plan Options**''). Only EMI options have been granted under the 2011 Plan. All 2011 Plan Options have been granted to Dr Stephen Franklin.

Pursuant to the Option Exchange Agreement, Dr Franklin exchanged his 2011 Plan Options for options over ordinary shares of £2 in the capital of the Company on the same terms as his 2011 Plan Options.

12.3.2 ***Outstanding Options***

As at the date of this document, there are 2011 Plan Options over 3,972,800 Ordinary Shares.

12.3.3 ***Eligibility***

2011 Plan Options can be granted to any employee of the Company and any subsidiary of the Company. EMI options can only be granted to eligible employees pursuant to Schedule 5 ITEPA, namely those whose committed time (for the purposes of Schedule 5 ITEPA) amounts to at least 25 hours a week or, if less, 75 per cent. of his working time and has no material interest (for the purposes of Schedule 5 ITEPA) in the Company.

12.3.4 ***Grant of Options***

2011 Plan Options can be granted at any time until 25 November 2021, being the tenth anniversary of date of adoption of the rules of the 2011 Plan unless the Company is prohibited from granting 2011 Plan Options by any law or regulation with the force of law, or where the grant of such options would be in breach of any such law or regulation.

12.3.5 ***Exercise Price***

The price per Ordinary Share ranges from £0.05 to £0.0265375. All 2011 Plan Options have been granted at (or more than) the market value per Ordinary Share as agreed with HM Revenue & Customs Shares and Assets Valuation division at the relevant time.

12.3.6 ***Individual limits on participation***

There are no individual limits on participation in the 2011 Plan, subject to the limit set out in Schedule 5 ITEPA at the date of grant which restricts the grant of EMI options (see paragraph 12.2.7 of this Part VI).

12.3.7 ***Limit on the issue of Shares***

The only limits applying to the grant of 2011 Plan Options are the applicable limits set out in Schedule 5 ITEPA for the grant of any EMI options (see paragraph 12.2.7 of this Part VI).

12.3.8 ***Sourcing the Option Shares***

The Company must allot and issue (or transfer, as appropriate) the Ordinary Shares acquired by optionholders within 30 days of exercise of their 2011 Plan Options.

12.3.9 ***Exercise and lapse of options***

Dr Franklin holds four 2011 Plan Options, with different exercise conditions:

(a) an option over 1,015,200 Ordinary Shares to replace a Evgen Option granted on 25 November 2011, which option is fully vested and exercisable;

(b) an option over 1,940,800 Ordinary Shares to replace a Evgen Option granted on 23 December 2013, which option is exercisable on a change of control, an asset sale, a listing of the Company's shares on a recognised stock exchange for the purposes of section 1137 of the Corporation Tax Act 2010 or on AIM, or an agreement for the licencing of Sulforadex®. The extent to which the option becomes exercisable depends on the value received by shareholders of the Company in connection with the event in question, with the option becoming fully vested and exercisable where the value of consideration received is £50 million or more. The Board has exercised its discretion in terms of the option agreement and determined that the option will become fully vested and exercisable on Admission;

(c) an option over 884,000 Ordinary Shares to replace a Evgen Option granted on 26 June 2015 which option itself replaced a Evgen Option granted on 18 August 2010 (and an Evgen Option granted on 21 November 2014) which becomes fully vested and exercisable on Admission; and

(d) an option over 132,800 Ordinary Shares to replace a Evgen Option granted on 26 June 2015 which option itself replaced a Evgen Option granted on 11 January 2011 (and an Evgen Option granted on 21 November 2014) which is already fully vested and exercisable.

The 2011 Plan Options lapse on the earliest of:

- 30 days after the date of grant if the optionholder does not enter into an option agreement and (unless the option is not intended to be an EMI option) correctly complete, sign and date an EMI notice for the purposes of notification of the EMI option to HMRC and return it to the Company, each within 30 days of the date of grant;
- any attempt by the optionholder to transfer, assign or have any charge or other security interest created over the 2011 Plan Option in question (or any right arising under it);
- the date on which any exercise condition applying to the whole 2011 Plan Option becomes incapable of being met, as a result of which no part of the 2011 Plan Option can be exercised. Where an exercise condition relates only to part of the 2011 Plan Option, that part shall lapse when the exercise condition is no longer capable of being met;
- any lapse date specified in the relevant 2011 Plan Option agreement;
- the first anniversary of the optionholder's death;
- 12 months after the optionholder ceases to be an employee of the Company (or any subsidiary) by reason of injury, ill health, disability, retirement or redundancy;
- the date that the Board specifies where an optionholder has ceased employment (other than by reason of death, injury, ill health, disability, retirement or redundancy) and the Board has allowed the 2011 Plan Option to be exercised during a specified period;
- where the Board does not determine that the 2011 Plan Option shall be exercisable following cessation of employment (see above), the earliest of three months following cessation or the date that the Board determines that the 2011 Plan Option shall not be so exercisable;
- the time when the company which employs the optionholder leaves the Group;
- the later of six weeks following a change of control and where the acquiring company is a company, the later of such date and the earlier of (i) the 2011 Plan Option is released under an exchange of options to which Part 6 of Schedule 5 ITEPA applies; and (ii) six months after the acquiring company obtains control of the Company (see paragraph 12.3.12 of this Part VI);
- one month following a person becoming bound or entitled to acquire shares in the Company under Chapter 3 of Part 28 of the Act and where the acquiring company is a company, the later of such date and the earlier of (i) the date that the relevant 2011 Plan Option is released under an exchange of options to which Part 6 of Schedule 5 ITEPA applies; and (ii) six months after the acquiring company obtains control of the Company (see paragraph 12.3.12 of this Part VI); and
- the time when the optionholder becomes bankrupt, applies for an interim order or makes a voluntary arrangement, in each case under the Insolvency Act 1996, or takes similar steps, or is similarly affected, under laws of any jurisdiction that corresponds to the relevant provisions of the Insolvency Act 1996.

12.3.10 ***Internal reconstruction***

Where the change of control provisions (see paragraph 12.3.12 of this Part VI) apply, an internal reorganisation may trigger exercise of the 2011 Plan Options. However, the Board, in its discretion can determine that the exercise, lapse and change of control provisions don't apply where there is a qualifying exchange of shares pursuant to Schedule 5 ITEPA or any other corporate reconstruction or reorganisation under which the ultimate beneficial ownership of the businesses of the Company remains the same and the exchange, reconstruction or reorganisation includes provisions which the Board, in its reasonable opinion, considers to be fair for the grant of replacement

options. Where the Board so determines, optionholders shall exchange their 2011 Plan Options for equivalent options in the acquiring company which, in the case of an EMI option, qualifies as a replacement option under Schedule 5 ITEPA or, in the case of an unapproved option, on terms which are agreed with the acquiring company.

12.3.11 ***Winding-up of the Company***

If the shareholders of the Company receive a notice for the voluntary winding up of the Company, the 2011 Plan Options may be exercised in the period before that resolution is withdrawn, rejected or passed.

12.3.12 ***Takeover of the Company***

If any person (i) makes an offer to acquire the whole of the issued share capital of the Company, (ii) makes an offer to acquire all of the shares of the same class as the option shares, namely the Ordinary Shares or (iii) negotiates a share sale and purchase agreement with the shareholders of the Company which contemplates that the offeror will obtain control of the Company on completion, the option may be exercised within a reasonable period specified by the Board for that purpose and ending immediately before change of control.

If any person has obtained control of the company as a result of (i) making an offer to acquire the whole of the issued share capital of the Company, (ii) making an offer to acquire all of the shares of the same class as the option shares, namely the Ordinary Shares or (iii) entering into a share sale and purchase agreement with the shareholders of the Company, the 2011 Plan Options may be exercised within six weeks of the change of control, at the end of which time it lapses unless the purchaser is a company. If the purchaser is a company, the 2011 Plan Options continue to exist until the earlier of (i) the date that the relevant 2011 Plan Option is released under an exchange of options to which Part 6 of Schedule 5 ITEPA applies and (ii) six months after the purchaser obtains control of the Company.

Unless the relevant compromise or arrangement includes provisions for the replacement of options or other compensation for the 2011 Plan optionholders for loss of the 2011 Plan Options, the 2011 Plan Options are exercisable within six weeks of any person obtaining control of the Company as a result of the court sanctioning a compromise or arrangement under Part 26 and (where applicable) Part 27 of the Act, at the end of which time it lapses unless the purchaser is a company. If the purchaser is a company, the 2011 Plan Options continue to exist until the earlier of (i) the date that the relevant 2011 Plan Option is released under an exchange of options to which Part 6 of Schedule 5 ITEPA applies and (ii) six months after the purchaser obtains control of the Company.

12.3.13 ***National Insurance Contributions (''NICs'')***

Unless the member of the Group which employs the optionholder directs otherwise, each 2011 Plan Option agreement shall include the optionholder's irrevocable agreement that the Company, the optionholder's employer or former employer may recover the whole or part of the employer's NICs payable in relation to the 2011 Plan Option and at the request of the Company, the optionholder shall elect (using a form approved by HMRC) that the whole or part of the employer's NICs shall be transferred to the optionholder.

Each option agreement shall include an irrevocable agreement to pay to the Company, the optionholder's employer or former employer any option tax liability, namely any income tax, employee's NICs and employer's NICs (if requested by the Company – see above) payable by the Company (or any other member of the Group). To the extent that the optionholder does not pay his option tax liability within seven days of exercise of his 2011 Plan Option, the Company may withhold sufficient shares from the option shares to be delivered to the optionholder and sell such shares to meet any option tax liability (paying the balance of any net proceeds to the optionholder).

12.3.14 ***Variation of Share Capital***

The Board shall adjust the number and description of shares subject to option and exercise price for each share under the 2011 Plan Option as it considers appropriate in the event of any variation of the share capital of the Company (whether that variation

is a capitalisation issue (other than a scrip dividend), rights issue, consolidation, subdivision or reduction of capital or otherwise) which affects the value of the 2011 Plan Options in a manner which, in its reasonable opinion, it considers to be fair and appropriate.

12.3.15 ***Amendment of the Share Scheme***

The Board may alter or add to the provisions of the 2011 Plan at any time provided that no amendment may be made without the prior approval of the Company in general meeting if it would make the terms on which 2011 Plan Options may be granted materially more generous, change the definition of eligible employee to expand the class of potential optionholders or change the variation of share capital provisions to the benefit of option holders unless any such amendments are minor to benefit administration of the 2011 Plan, to take account of any change in legislation or to obtain or maintain favourable tax, exchange control or regulatory treatment for optionholders or any member of the Company's Group.

12.4 ***Standalone Unapproved Agreements***

12.4.1 ***Outline***

Unapproved share options over Evgen shares were granted to employees and directors of Evgen by way of Standalone Unapproved Agreements from November 2011 onwards (the "**Unapproved Options**").

Pursuant to the Option Exchange Agreement, employees and directors holding Unapproved Options exchanged their Unapproved Options over ordinary shares in the capital of Evgen for a corresponding number of Unapproved Options over Ordinary Shares.

12.4.2 ***Outstanding Options***

As at the date of this document, there are Unapproved Options over 1,864,800 Ordinary Shares.

12.4.3 ***Exercise Price***

The price per Ordinary Share payable ranges from £0.00875 to £0.10615.

12.4.4 **Sourcing the Option Shares**

The Company must allot and issue the Ordinary Shares acquired by optionholders within 30 days of exercise of their Unapproved Options.

12.4.5 ***Exercise and lapse of options***

All of the Unapproved Options become exercisable following the Admission (to the extent that they were not already exercisable).

The Unapproved Options lapse on the earliest of:-

- 30 days after the date of grant if the optionholder does not enter into an option agreement;
- any attempt by the optionholder to transfer, assign or have any charge or other security interest created over the Unapproved Option in question (or any right arising under it);
- the first anniversary of the optionholder's death; and
- the time when the optionholder becomes bankrupt, applies for an interim order or makes a voluntary arrangement, in each case under the Insolvency Act 1996, or takes similar steps, or is similarly affected, under laws of any jurisdiction that corresponds to the relevant provisions of the Insolvency Act 1996.

12.4.6 ***Winding-up of the Company***

If the Company passes or is about to pass a resolution for voluntary winding-up, the Company shall notify the optionholders in advance of the winding-up and the Unapproved Options may be exercised following the voluntary winding-up. There is no provision for the Unapproved Options to lapse following a voluntary winding-up of the Company.

12.4.7 ***Takeover of the Company***

If an unconditional offer is made to acquire control of the Company which is accepted by the shareholders of the Company, the Company shall notify the optionholders in advance of the change of control and the Unapproved Options may be exercised following the change of control. There is no provision for the Unapproved Options to lapse following a change of control of the Company.

12.4.8 ***National Insurance Contributions (''NICs'')***

There are no provisions for income tax or NICs in any of the Unapproved Options agreements with the exception of Joanne Lishman's option. Joanne Lishman's option agreement grants an indemnity from Ms Lishman in favour of the Company in relation to any income tax or employee's NICs payable in respect of her Unapproved Option.

The Company (or the optionholder's employer, if different) will be liable for the payment of any employer's NICs arising in respect of all of the Unapproved Options.

12.4.9 ***Variation of Share Capital***

The Board shall adjust the number and description of shares subject to option and exercise price for each share under the Unapproved Options agreements as it considers appropriate in the event of any variation of the share capital of the Company (whether that variation is a capitalisation issue (other than a scrip dividend), rights issue, consolidation, subdivision or reduction of capital or otherwise) which affects the value of the Unapproved Options in a manner which, in its reasonable opinion, it considers to be fair and appropriate.

12.5 ***Long-term incentive plan (''LTIP'')***

12.5.1 ***LTIP Outline***

The LTIP, which is to be adopted by the Company conditional upon Admission, is a discretionary executive share plan. Under the LTIP, the Board may, within certain limits and subject to any applicable performance conditions, grant to eligible employees (i) options over Ordinary Shares (''**LTIP Options**'') and/or (ii) conditional awards (i.e. a conditional right to acquire Ordinary Shares) (''**LTIP Conditional Awards**'') and/or (iii) Ordinary Shares which are subject to restrictions and the risk of forfeiture (''**LTIP Restricted Shares**''), together with LTIP Options and LTIP Conditional Awards, an ''**LTIP Award**''. No payment is required for the grant of an LTIP Award.

The exercise price payable for each Ordinary Share subject to an LTIP Option shall be determined by the Board and may be nil.

Awards are not transferable other than to the participant's personal representatives in the event of his death provided that awards and Ordinary Shares may be held by the trustees of an employee as nominee for the participants.

12.5.2 ***Eligibility***

All employees of the Group are eligible for selection to participate in the LTIP at the discretion of the Board.

12.5.3 ***Grant of LTIP Awards***

LTIP Awards may be granted during the 42 days beginning on: (i) Admission; (ii) the day after the announcement of the Company's results for any period; (iii) any day on which the Board determines that circumstances are sufficiently exceptional to justify the making of the LTIP Award at that time; or (iv) the day after the lifting of any dealing restrictions. However, no LTIP Awards may be granted more than ten years from the date when the LTIP was adopted.

12.5.4 ***Individual limits on participation***

The Board may grant annually LTIP Awards over Ordinary Shares to eligible employees with a maximum total market value of up to 100 per cent. of the relevant individual's annual base salary subject to a higher limit of 150 per cent. of the relevant individual's annual base salary in circumstances that the Board determines are exceptional.

In addition, the Board may grant the first LTIP Awards (the "**LTIP IPO Awards**") outside these limits over Ordinary Shares to eligible employees with a maximum total market value of up to 300 per cent. of the relevant individual's annual base salary. The Board reserves the right to calculate market value by reference to the Placing Price for the purposes of these LTIP IPO Awards. The Board has made LTIP IPO Awards to Barry Clare and Stephen Franklin, conditional on Admission, over Ordinary Shares with a total market value of 300 per cent. of the relevant individual's annual base salary by reference to the Placing Price. One-third of the LTIP IPO Awards to Barry Clare and Stephen Franklin will vest conditional on Admission, one-third on the first anniversary of Admission and one-third on the third anniversary of Admission. The Board has made LTIP IPO Awards to John Bradshaw over Ordinary Shares with a total market value of 50 per cent. of his annual base salary by reference to the Placing Price. The LTIP IPO Awards for John Bradshaw will vest on the first anniversary of Admission. The Board has made LTIP IPO Awards to further two employees over Ordinary Shares with a total market value of £37,000 by reference to the Placing Price. One-half of such LTIP IPO Awards will vest conditional on Admission and the other half will vest on the first anniversary of Admission.

12.5.5 ***Limit on the issue of Ordinary Shares***

The rules of the LTIP provide that, in any period of 10 calendar years, not more than 10 per cent. of the Company's issued ordinary share capital may be issued under the LTIP and under any other employees' share scheme operated by the Company. Ordinary Shares issued out of treasury under the LTIP will count towards these limits for so long as this is required under institutional shareholder guidelines. Ordinary Shares issued or to be issued pursuant to options granted before Admission and pursuant to the LTIP IPO Awards will not count towards these limits. In addition, awards which are renounced or lapse shall be disregarded for the purposes of these limits.

12.5.6 ***Sourcing the Ordinary Shares***

The LTIP may operate over new issue Ordinary Shares, treasury Ordinary Shares or Ordinary Shares purchased in the market. The Company may establish an employee trust in the future which may be funded by one or more members of the Group to acquire Ordinary Shares.

12.5.7 ***Performance and other conditions***

The Board may impose performance conditions on the vesting of LTIP Awards. Where performance conditions are specified for LTIP Awards, the underlying measurement period for such conditions will ordinarily be three years.

The proposed performance conditions for the first grant of LTIP Awards will have one performance condition with the LTIP Award vesting based on absolute total shareholder return targets over a period of three years from the date of grant of the relevant LTIP Award.

Any performance conditions applying to LTIP Awards may be varied, substituted or waived if the Board considers it appropriate, provided the Board considers that the new performance conditions are reasonable and are not materially less difficult to satisfy than the original conditions (except in the case of waiver).

The Board may also impose other conditions on the vesting of LTIP Awards.

12.5.8 ***Malus***

The Board may decide, at any time prior to the vesting of LTIP Awards, that the number of Ordinary Shares subject to an LTIP Award shall be reduced (including to nil) on such basis that the Board in its discretion considers to be fair and reasonable where the Board determines:

- there has been a material misstatement resulting in an adjustment of the audited accounts of the Group or any Group company;
- that the assessment of any performance condition in respect of an LTIP Award was based on error, or inaccurate or misleading information;

- that any information used to determine the number of Ordinary Shares subject to an LTIP Award was based on error, or inaccurate or misleading information;
- that there has been action or conduct of a participant which amounts to gross misconduct; or
- that events or the behaviour of a participant have led to the censure of a member of the Group by a regulatory authority or have had a significant detrimental impact on the reputation of any member of the Group provided that the Board is satisfied that the relevant participant was responsible for the censure or reputational damage and that the censure or reputational damage is attributable to him.

12.5.9 ***Vesting and exercise***

LTIP Awards will normally vest, and LTIP Options will normally become exercisable, on the third anniversary of the date of grant of the LTIP Award to the extent that any applicable performance conditions have been satisfied and to the extent permitted following any operation of malus or clawback. LTIP Options will normally remain exercisable for a period determined by the Board at grant, which shall not exceed 10 years from grant.

12.5.10 ***Holding period***

At its discretion, the Board may grant LTIP Awards subject to a holding period of a maximum of two years following vesting.

12.5.11 ***Cessation of employment***

Except in certain circumstances, set out below, an LTIP Award will lapse immediately upon a participant ceasing to be employed by or holding office with the Group.

If a participant so ceases because of his ill-health, injury, disability, redundancy, retirement with the agreement of his employer, the participant being employed by a company which ceases to be a member of the Group or being employed in an undertaking which is transferred to a person who is not a member of the Group or in other circumstances at the discretion of the Board (each an "**LTIP Good Leaver Reason**"), his LTIP Award will ordinarily vest on the date when it would have vested if he had not so ceased to be a Group employee or director, subject, unless the Board decides otherwise, to the satisfaction of any applicable performance conditions measured over the original performance period and the operation of malus or clawback. In addition, unless the Board decides otherwise, vesting will be pro-rated to reflect the reduced period of time between grant and the participant's cessation of employment as a proportion of the normal vesting period.

The Board can alternatively decide that the LTIP Award of a participant who has ceased to be a Group employee or director for an LTIP Good Leaver Reason will vest early when he leaves. If a participant dies, a proportion of his LTIP Award will vest on the date of his death. The extent to which an LTIP Award will vest in these situations will be determined by the Board at its absolute discretion taking into account the period of time the LTIP Award has been held and the extent to which any applicable performance conditions have been satisfied at the date of cessation of employment and the operation of malus or clawback. In addition, unless the Board decides otherwise, vesting will be pro-rated to reflect the reduced period of time between grant and the participant's cessation of employment as a proportion of the normal vesting period.

To the extent that LTIP Options vest for an LTIP Good Leaver Reason, they may be exercised for a period of six months following vesting (or such longer period as the Board determines) and will otherwise lapse at the end of that period. To the extent that LTIP Options vest following death of a participant, they may be exercised for a period of 12 months following death and will otherwise lapse at the end of that period.

12.5.12 ***Clawback***

The Board may apply clawback to all or part of a participant's LTIP Award in similar circumstances as apply under malus (see paragraph 12.5.8 of this Part VI) during the period of three years (or such other period not exceeding three years as the Board

may determine) following vesting of the LTIP Award. Clawback may be effected, among other means, by requiring the transfer of Ordinary Shares, payment of cash or reduction of other awards or bonuses.

12.5.13 ***Corporate events***

In the event of a takeover, scheme of arrangement or winding-up of the Company, the LTIP Awards will vest early. The extent to which the LTIP Awards will vest shall be determined by the Board taking into account, unless the Board decides otherwise, the extent to which any applicable performance conditions have been satisfied at that time.

To the extent that LTIP Options vest in the event of a takeover, winding-up or scheme of arrangement of the Company they may be exercised for a period of six months measured from the relevant event (or in the case of takeover such longer period as the Board determines) and will otherwise lapse at the end of that period.

In the event of a demerger, distribution or any other corporate event, the Board may determine that LTIP Awards shall vest. The proportion of the LTIP Awards which will vest shall be determined by the Board taking into account, unless the Board decides otherwise, the extent to which any applicable performance conditions have been satisfied at that time. LTIP Options that vest in these circumstances may be exercised during such period as the Board determines and will otherwise lapse at the end of that period.

If there is a corporate event resulting in a new person or company acquiring control of the Company, the Board may (with the consent of the acquiring company) alternatively decide that LTIP Awards will not vest or lapse but will be replaced by equivalent new awards over shares in the new acquiring company.

12.5.14 ***Variation of capital***

If there is a variation of share capital of the Company or in the event of a demerger or other distribution, special dividend or distribution, the Board may make such adjustments to LTIP Awards, including the number of Ordinary Shares subject to LTIP Awards and the option exercise price (if any), as it considers to be fair and reasonable.

12.5.15 ***Dividend equivalents***

In respect of any LTIP Award, the Board may decide that participants will receive a payment (in cash and/or additional Ordinary Shares) equal in value to any dividends that would have been paid on the Ordinary Shares which vest under that award by reference to the period between the time when the relevant award was granted and the time when the relevant award vested. This amount may assume the reinvestment of dividends and exclude or include special dividends or dividends in specie.

12.5.16 ***Alternative settlement***

At its discretion, the Board may decide to satisfy LTIP Awards grants with a cash payment equal to any gain that a participant would have made had the relevant award been satisfied with Ordinary Shares.

12.5.17 ***Rights attaching to Ordinary Shares***

Except in relation to the award of Ordinary Shares subject to restrictions, Ordinary Shares issued and/or transferred under the LTIP will not confer any rights on any participant until the relevant award has vested or the relevant option has been exercised and the participant in question has received the underlying Ordinary Shares. Any Ordinary Shares allotted when an option is exercised or an award vests will rank equally with Ordinary Shares then in issue (except for rights arising by reference to a record date prior to their issue). A participant awarded Ordinary Shares subject to restrictions shall have the same rights as a holder of Ordinary Shares in issue at the time that the participant acquires the Ordinary Shares, save to the extent set out in the agreement with the participant relating to those Ordinary Shares.

12.5.18 ***Benefits not pensionable***

The benefits received under the LTIP are not pensionable.

12.5.19 ***Overseas plans***

The Board may, at any time, establish further plans based on the LTIP for overseas territories. Any such plan shall be similar to the LTIP, as relevant, but modified to take account of local tax, exchange control or securities laws. Any Ordinary Shares made available under such further overseas plans must be treated as counting against the limits on individual and overall participation under the LTIP.

12.5.20 ***Amendments***

The Board may, at any time, amend the provisions of the LTIP in any respect. The prior approval of shareholders at a general meeting of the Company must be obtained in the case of any amendment to the material advantage of participants which is made to the provisions relating to eligibility, individual or overall limits, the persons to whom an award can be made under the LTIP, the adjustments that may be made in the event of any variation to the share capital of the Company and/or the rule relating to such prior approval, save that there are exceptions for any minor amendment to benefit the administration of the LTIP, to take account of the provisions of any proposed or existing legislation or to obtain or maintain favourable tax, exchange control or regulatory treatment for participants, the Company and/or its other Group companies. Amendments may not normally adversely affect the rights of participants except where participants are notified of such amendment and the majority of participants approve such amendment.

12.6 ***DBP share plan***

12.6.1 ***DBP Outline***

The DBP, which is to be adopted by the Company conditional upon Admission, is a discretionary executive share plan. Under the DBP, the Board may, within certain limits, grant to eligible employees (i) nil cost options over Ordinary Shares ("**DBP Options**") and/or (ii) conditional awards (i.e. a conditional right to acquire Ordinary Shares) ("**DBP Conditional Awards**") and/or (iii) Ordinary Shares which are subject to restrictions and the risk of forfeiture ("**DBP Restricted Shares**" and, together with DBP Options and DBP Conditional Awards, a "**DBP Award**"). No payment is required for the grant of a DBP Award.

Awards are not transferable other than to the participant's personal representatives in the event of his death provided that awards and Ordinary Shares may be held by the trustees of an employee as nominee for the participants.

12.6.2 ***Eligibility***

All employees of the Group are eligible for selection to participate in the DBP at the discretion of the Board.

12.6.3 ***Grant of DBP Awards***

The Board may determine that a proportion of a participant's annual bonus will be deferred into a DBP Award.

There is a maximum limit on the market value of Ordinary Shares granted to any employee under a DBP Award of 50 per cent. of the total annual bonus for that individual. DBP Awards may be granted during the 42 days beginning on: (i) Admission; (ii) the day after the announcement of the Company's results for any period; (iii) any day on which the Board determines that circumstances are sufficiently exceptional to justify the making of the DBP Award at that time; or (iv) the day after the lifting of any dealing restrictions.

However, no DBP Awards may be granted more than 10 years from the date when the DBP was adopted.

12.6.4 ***Limit on the issue of Ordinary Shares***

The rules of the DBP provide that, in any period of 10 calendar years, not more than 10 per cent. of the Company's issued ordinary share capital may be issued under the DBP and under any other employees' share scheme operated by the Company. Ordinary Shares issued out of treasury under the DBP will count towards these limits for so long as this is required under institutional shareholder guidelines. Ordinary Shares issued or to be issued pursuant to options granted before Admission or

pursuant to the LTIP IPO Awards will not count towards these limits. In addition, awards which are renounced or lapse shall be disregarded for the purposes of these limits.

12.6.5 ***Sourcing the Ordinary Shares***

The DBP may operate over new issue Ordinary Shares, treasury Ordinary Shares or Ordinary Shares purchased in the market. The Company may establish an employee trust in the future which may be funded by one or more members of the Group to acquire Ordinary Shares.

12.6.6 ***Malus***

The Board may decide, at any time prior to the vesting of DBP Awards, that the number of Ordinary Shares subject to a DBP Award shall be reduced (including to nil) on such basis that the Board in its discretion considers to be fair and reasonable where the Board determines:

- there has been a material misstatement resulting in an adjustment of the audited accounts of the Group or any Group company;
- that the assessment of any performance condition in respect of an DBP Award was based on error, or inaccurate or misleading information;
- that any information used to determine the number of Ordinary Shares subject to an DBP Award was based on error, or inaccurate or misleading information;
- that there has been action or conduct of a participant which amounts to gross misconduct; or
- that events or the behaviour of a participant have led to the censure of a member of the Group by a regulatory authority or have had a significant detrimental impact on the reputation of any member of the Group provided that the Board is satisfied that the relevant participant was responsible for the censure or reputational damage and that the censure or reputational damage is attributable to him.

12.6.7 ***Vesting and exercise***

DBP Awards will normally vest, and DBP Options will normally become exercisable on the third anniversary of the date of grant of the DBP Award to the extent permitted following any operation of malus or clawback. DBP Options will normally remain exercisable for a period determined by the Board at grant which shall not exceed 10 years from grant.

12.6.8 ***Holding period***

At its discretion, the Board may grant DBP Awards subject to a holding period of a maximum of two years following vesting.

12.6.9 ***Cessation of employment***

Except in certain circumstances, set out below, a DBP Award will lapse immediately upon a participant ceasing to be employed by or holding office with the Group.

However, if a participant so ceases because of his ill-health, injury, disability, redundancy, retirement with the agreement of his employer, the participant being employed by a company which ceases to be a member of the Group or being employed in an undertaking which is transferred to a person who is not a member of the Group or in other circumstances at the discretion of the Board (each an "**DBP Good Leaver Reason**"), his DBP Award will ordinarily vest on the date when it would have vested if he had not so ceased to be a Group employee or director, subject to the operation of malus or clawback. In addition, unless the Board decides otherwise, vesting will be pro-rated to reflect the reduced period of time between grant and the participant's cessation of employment as a proportion of the normal vesting period.

If a participant ceases to be a Group employee or director for a DBP Good Leaver Reason, the Board can alternatively decide that his DBP Award will vest early when he leaves. If an employee dies, a proportion of his DBP Award will vest on the date of his death. The extent to which a DBP Award will vest in these situations will be determined by the Board at its absolute discretion taking into account, among other factors, the period of time the DBP Award has been held and the operation of malus or

clawback. In addition, unless the Board decides otherwise, vesting will be pro-rated to reflect the reduced period of time between grant and the participant's cessation of employment as a proportion of the normal vesting period.

To the extent that DBP Options vest for a DBP Good Leaver Reason, they may be exercised for a period of six months following vesting (or such longer period as the Board determines) and will otherwise lapse at the end of that period. To the extent that DBP Options vest following death of a participant, they may be exercised for a period of 12 months following death and will otherwise lapse at the end of that period.

12.6.10 ***Clawback***

The Board may apply clawback to all or part of a participant's DBP Award in similar circumstances as apply under malus (see paragraph 12.6.6 of this Part VI above) during the period of three years following the determination of the bonus by reference to which the DBP Award was granted. Clawback may be effected, among other means, by requiring the transfer of Ordinary Shares, payment of cash or reduction of awards or bonuses.

12.6.11 ***Corporate events***

In the event of a takeover, scheme of arrangement or winding-up of the Company, the DBP Awards will vest early. The extent to which the DBP Awards will vest shall be determined by the Board taking into account, among other factors, the period of time the DBP Award has been held by the participant.

To the extent that DBP Options vest in the event of a takeover, winding-up or scheme of arrangement of the Company they may be exercised for a period of six months measured from the relevant event (or in the case of takeover such longer period as the Board determines) and will otherwise lapse at the end of that period.

In the event of a demerger, distribution or any other corporate event, the Board may determine that DBP Awards shall vest. The proportion of the DBP Awards which will vest shall be determined by the Board taking into account, among other factors, the period of time the DBP Award has been held by the participant. DBP Options that vest in these circumstances may be exercised during such period as the Board determines and will otherwise lapse at the end of that period.

If there is a corporate event resulting in a new person or company acquiring control of the Company, the Board may (with the consent of the acquiring company) alternatively decide that DBP Awards will not vest or lapse but will be replaced by equivalent new awards over shares in the new acquiring company.

12.6.12 ***Variation of capital***

If there is a variation of share capital of the Company or in the event of a demerger or other distribution, special dividend or distribution, the Board may make such adjustments to DBP Awards, including the number of Ordinary Shares subject to DBP Awards and the option exercise price (if any), as it considers to be fair and reasonable.

12.6.13 ***Dividend equivalents***

In respect of any DBP Award, the Board may decide that participants will receive a payment (in cash and/or additional Ordinary Shares) equal in value to any dividends that would have been paid on the Ordinary Shares which vest under that award by reference to the period between the time when the relevant award was granted and the time when the relevant award vested. This amount may assume the reinvestment of dividends and exclude or include special dividends or dividends in specie.

12.6.14 ***Alternative settlement***

At its discretion, the Board may decide to satisfy DBP Awards with a cash payment equal to any gain that a participant would have made had the relevant award been satisfied with Ordinary Shares.

12.6.15 ***Rights attaching to Ordinary Shares***

Except in relation to the award of Ordinary Shares subject to restrictions, Ordinary Shares issued and/or transferred under the DBP will not confer any rights on any participant until the relevant award has vested or the relevant option has been

exercised and the participant in question has received the underlying Ordinary Shares. Any Ordinary Shares allotted when an option is exercised or an award vests will rank equally with Ordinary Shares then in issue (except for rights arising by reference to a record date prior to their issue). A participant awarded Ordinary Shares subject to restrictions shall have the same rights as a holder of Ordinary Shares in issue at the time that the participant acquires the Ordinary Shares, save to the extent set out in the agreement with the participant relating to those Ordinary Shares.

12.6.16 ***Benefits not pensionable***

The benefits received under the DBP are not pensionable.

12.6.17 ***Overseas plans***

The Board may, at any time, establish further plans based on the DBP for overseas territories. Any such plan shall be similar to the DBP, as relevant, but modified to take account of local tax, exchange control or securities laws. Any Ordinary Shares made available under such further overseas plans must be treated as counting against the limits on individual and overall participation under the DBP.

12.6.18 ***Amendments***

The Board may, at any time, amend the provisions of the DBP in any respect. The prior approval of shareholders at a general meeting of the Company must be obtained in the case of any amendment to the material advantage of participants which is made to the provisions relating to eligibility, individual or overall limits, the persons to whom an award can be made under the DBP, the adjustments that may be made in the event of any variation to the share capital of the Company and/or the rule relating to such prior approval, save that there are exceptions for any minor amendment to benefit the administration of the DBP, to take account of the provisions of any proposed or existing legislation or to obtain or maintain favourable tax, exchange control or regulatory treatment for participants, the Company and/or its other Group companies. Amendments may not normally adversely affect the rights of participants except where participants are notified of such amendment and the majority of participants approve such amendment.

13. LITIGATION

The Group is not, nor has at any time in the twelve months immediately preceding the date of this document, been engaged in any governmental, legal or arbitration proceedings and the Directors are not aware of any governmental, legal or arbitration proceedings pending or threatened by or against the Group, nor of any such proceedings having been pending or threatened at any time in the twelve months preceding the date of this document in each case which may have, or have had in the twelve months preceding the date of this document, a significant effect on the Group's financial position or profitability.

14. DIRECTORS' DEALINGS

The Directors intend to comply with Rule 21 of the AIM Rules relating to directors' dealings as applicable to AIM companies and will also take all reasonable steps to ensure compliance by the Company's applicable employees (as defined in the AIM Rules).

15. RELATED PARTY TRANSACTIONS

15.1 Save as disclosed in this document, as far as the Directors are aware there have been and are currently no agreements or other arrangements between the Company and individuals or entities that may be deemed to be related parties, for the period of five years prior to the date of this document.

15.2 The members of the Group have entered into the following transactions with related parties during the period covered by the Historical Financial Information set out in Part III of this document and up to the date of this document. These transactions as a whole were conducted on arm's length terms (or terms which were not on arm's length terms but more favourable terms from the Company's perspective) and are considered material in the context of the turnover of the Group in the relevant periods:

15.2.1 on 5 December 2014, the Company entered into a deed of adherence, variation and termination of the Investment Agreement, further details of which are set out in paragraph 10.1 of this Part VI;

15.2.2 on 14 October 2015, the Company entered into the NWFB Relationship Agreement, further details of which are set out in paragraph 10.2 of this Part VI;

15.2.3 on 5 December 2014, the Company entered into the Share for Share Exchange Agreement, further details of which are set out in paragraph 10.3 of this Part VI;

15.2.4 on 25 June 2015, the Company entered into the Option Exchange Agreements, further details of which are set out in paragraph 10.4 of this Part VI;

15.2.5 on 14 October 2015, the Company entered into the Hard Lock-in and Orderly Market Agreements, further details of which are set out in paragraph 10.6 of this Part VI;

15.2.6 on 14 October 2015, the Company entered into the Soft Lock-in and Orderly Market Agreements further details of which are set out on paragraph 10.7 of this Part VI;

15.2.7 on 2 July 2013, the Company entered into the 2013 Subscription Agreement, further details of which are set out in paragraph 10.12 of this Part VI;

15.2.8 on 3 November 2014, the Company entered into the 2014 Subscription Agreement, further details of which are set out in paragraph 10.15 of this Part VI;

15.2.9 on 25 June 2015, the Company entered into the 2013 Loan Note Deed of Novation, further details of which are set out in paragraph 10.14 of this Part VI;

15.2.10 on 25 June 2015, the Company entered into the 2014 Loan Note Deed of Novation, further details of which are set out in paragraph 10.17 of this Part VI; and

15.2.11 on 26 August 2015, the Company allotted 9,569 ordinary shares of £2.00 each pursuant to the Pre-IPO Round, further details of which are set out in paragraph 10.19 of this Part VI.

Please also refer to the ''related party transactions'' set out in Section A of Part III of this document for further details of related party transactions.

16. WORKING CAPITAL

The Directors are of the opinion that, having made due and careful enquiry, the working capital available to the Group, taking into account the net proceeds of the Placing, will be sufficient for its present requirements, that is for at least 12 months from the date of Admission.

17. UNITED KINGDOM TAXATION

17.1 ***General***

17.1.1 The following paragraphs are intended as a general guide only and summarise advice received by the Directors about the UK tax position of Shareholders who are resident in the UK, holding shares as investments and not as securities to be realised in the course of a trade. They do not deal with the implications for Shareholders who acquire any shares or rights over shares in connection with an employment contract. The paragraphs below are based on current UK legislation and HMRC practice. It should be noted that although a number of UK tax treatments referred to below refer to unquoted shares, shares on AIM are generally treated as unquoted for these purposes.

17.1.2 Any person who is in any doubt about their tax position or who is subject to taxation in a jurisdiction other than the UK should consult their own professional adviser.

17.1.3 The information in these paragraphs is intended as a general summary of the UK tax position and should not be construed as constituting advice.

17.2 ***Taxation of dividends***

17.2.1 Any UK resident Shareholder who receives a dividend paid by the Company will be liable to UK income tax on the gross amount of any such dividend. Dividend income from the Company will be treated as forming the highest part of a Shareholder's income. The income tax rates are 10 per cent., 32.5 per cent. or 37.5 per cent. depending on the taxable income of the individual, but a deemed tax credit of 10 per cent. of the deemed dividend is to arise, the effect of which is to reduce the effective tax rates to 0 per cent., 25 per cent. and approximately 30.6 per cent. respectively.

Proposed changes to the taxation of dividend income were announced in the Summer Budget 2015. Should these proposed changes become law, a new dividend tax allowance of £5,000 per year will be available to individuals from 6 April 2016. The allowance will replace the existing dividend tax credit. The rates of tax on dividends are also expected to increase. The income tax rates are expected to be 7.5 per cent., 32.5 per cent. or 38.1 per cent. depending on the taxable income of the individual.

17.2.2 UK resident shareholders who do not pay income tax or whose liability to income tax on the dividend and related tax credit is less than the tax credit, are not entitled to claim repayment of any part of the tax credit associated with the dividend from HMRC.

17.2.3 A UK-tax resident corporate holder of non-redeemable ordinary shares in the Company that receives a dividend paid by the Company will not be subject to corporation tax in respect of that dividend subject to certain exceptions.

17.2.4 UK resident trustees of discretionary trusts receiving dividends from shares are also liable to account for income tax at the dividend trust rate, currently 10 per cent. or 37.5 per cent. depending on the taxable income of the trust. Although no specific guidance has yet been issued, the taxation of dividends may also affect trustees.

17.2.5 Whether a shareholder who is not resident in the UK for tax purposes is entitled to a tax credit in respect of dividends paid by the Company and to claim payment of any part of the tax credit will depend, in general, on the provisions of any double taxation convention which exists between the shareholder's country of residence and the UK. A non-UK resident shareholder may also be subject to foreign taxation on dividend income.

17.2.6 Persons who are not resident in the UK should consult their own tax advisers on the possible application of such provisions or what relief or credit may be claimed in the jurisdiction in which they are resident.

17.3 ***Taxation of chargeable gains***

17.3.1 For the purpose of UK tax on chargeable gains, the issue of New Ordinary Shares pursuant to the Placing will be regarded as an acquisition of a new holding in the share capital of the Company.

17.3.2 The Ordinary Shares so allotted will, for the purpose of tax on chargeable gains, be treated as acquired on the date of allotment. The amount paid for the Ordinary Shares will usually constitute the base cost of a Shareholder's holding.

17.3.3 If a Shareholder disposes of all or some of his or her Ordinary Shares, a liability to tax on chargeable gains may, depending on their circumstances and subject to any available exemptions or reliefs, arise.

17.3.4 A UK resident and domiciled individual Shareholder who disposes (or is deemed to dispose) of all or any of their shares may be liable to capital gains tax in relation thereto at rates up to 28 per cent., subject to any available exemptions or reliefs. In addition, an individual UK Shareholder who ceases to be resident in the UK for a period of less than five complete tax years and who disposes of the shares held prior to departure during that period of temporary non residence may, under anti-avoidance legislation, be liable to capital gains tax on his or her return to the UK.

17.3.5 A UK resident corporate Shareholder disposing of its shares in the Company may be liable to corporation tax on chargeable gains arising on the disposal at the corporation tax rate applicable to its taxable profits.

17.3.6 In computing the chargeable gain liable to corporation tax, the corporate Shareholder is entitled to deduct from the disposal proceeds the cost to it of the shares together with incidental costs of acquisition, as increased by an indexation allowance to adjust for inflation, and disposal costs.

17.3.7 The UK operates a substantial shareholding exemption regime which may apply to the disposal of shares in the Company by corporate shareholders, subject to certain conditions being met.

17.4 ***Inheritance tax***

17.4.1 Individuals and trustees subject to inheritance tax in relation to a shareholding in the Company may be entitled to business property relief of up to 100 per cent. after a holding period of two years providing that all the relevant conditions for the relief are satisfied at the appropriate time.

17.4.2 You should consult your taxation adviser if you are concerned with the potential inheritance tax implications of your shares in the Company.

17.5 ***Stamp Duty and Stamp Duty Reserve Tax***

17.5.1 No stamp duty or stamp duty reserve tax (''SDRT'') will generally be payable on the issue of the New Ordinary Shares.

17.5.2 If you are in any doubt as to your tax position, or are subject to tax in a jurisdiction other than in the UK, you should consult your professional adviser immediately.

17.5.3 With effect from 28 April 2014, stamp duty and SDRT was abolished on transactions on shares that are admitted to trading on a recognised growth market, including AIM, but not listed on any other market.

17.6 ***EIS and VCT***

17.6.1 ***Venture Capital Trusts***

The Company has applied for and obtained advance assurance from HMRC that the Placing Shares will be eligible shares for the purposes of the investment by VCTs. The status of the Placing Shares as a qualifying holding for VCTs will be conditional, *inter alia*, upon the Company continuing to satisfy the relevant requirements. It is the Directors' intention that the Company will continue to meet the Venture Capital Trust provisions so that it continues to be a qualifying company for these purposes. However, the Directors cannot give any warranty or undertaking that the Company will continue to meet the conditions, including in the event that the Directors believe that the interests of the Company are not best served by preserving the Venture Capital Trust status, or as a result of changes in legislation.

17.6.2 ***EIS***

The Company has applied for and obtained advance assurance from HMRC that a subscription for Placing Shares will be eligible for EIS purposes, subject to the submission of the relevant claim form in due course. The obtaining of such provisional assurance and submission of such a claim by the Company does not guarantee EIS qualification for an individual, whose claim for relief will be conditional upon his or her own circumstances and is subject to holding the shares throughout the relevant three year period.

In addition, for EIS relief not to be withdrawn, the Company must comply with a number of conditions throughout the qualifying period relating to those shares.

The following provides an outline of the EIS tax reliefs available to individuals and trustee investors. Any potential investor should obtain independent advice from a professional advisor in relation to their own particular set of personal circumstances.

In summary, EIS relief may be available where a qualifying company issues new shares, the purpose of which is to raise money for a qualifying business activity which can include that of research and development. The EIS shares must be subscribed for in cash and be fully paid up at the date of issue and must be held, broadly, for three years after they were issued.

EIS income tax relief is available to individuals only – the current relief is 30 per cent. of the amount subscribed for EIS shares to be set against the individual's income tax liability for the tax year in which the EIS investment is made, and is available up to a maximum of £1,000,000 in EIS subscriptions per tax year. This relief can be 'carried back' one tax year. This relief is only available to individuals who are not connected with the Company in the period of two years prior to and three years after the subscription.

Very broadly, an individual is connected with the issuing company if, *inter alia*, he or his associates are employees or directors or have an interest in more than 30 per cent. of the Company's ordinary share capital.

Where EIS income tax relief has been given and has not been withdrawn, any gain on the subsequent disposal of the shares in qualifying circumstances is generally free from capital gains tax. If the shares are disposed of at a loss, capital gains tax relief will generally be available for that loss net of any income tax relief previously given. Alternatively, an election can be made to set that loss (less any income tax relief already given) against income of that year.

Individuals and trustees who have realised gains on other assets within one year before or up to three years after the EIS shares are issued, are able to defer a capital gains tax liability arising on those gains by making a claim to reinvest an amount of those gains against the cost of the EIS share subscription. Deferred gains will become chargeable on a disposal or deemed disposal of the EIS shares. The investor can be connected with the Company (as outlined above) and obtain such capital gains tax deferral relief.

17.7 ***Summary***

The above is a summary of certain aspects of current law and practice in the UK. A Shareholder who is in any doubt as to his or her tax position and/or who is subject to tax in a jurisdiction other than the UK, should consult his or her professional adviser.

Any tax treatment referred to in this document depends on the individual circumstances of each investor and may be subject to change.

18. CREST

18.1 CREST is a paperless settlement system enabling securities to be evidenced otherwise than by a certificate and transferred otherwise than by written instrument in accordance with the CREST Regulations.

18.2 The Ordinary Shares will be eligible for CREST settlement. Accordingly, following Admission, settlement of transactions in the Ordinary Shares may take place within the CREST system if a Shareholder so wishes. CREST is a voluntary system and Shareholders who wish to receive and retain share certificates are able to do so.

18.3 For more information concerning CREST, Shareholders should contact their brokers or Euroclear UK & Ireland Limited at 33 Cannon Street, London EC4M 5SB or by telephone on +44 (0) 20 7849 0000.

19. GENERAL

19.1 The gross proceeds of the Placing receivable by the Company are expected to amount to approximately £7 million. Total costs and expenses payable by the Company in connection with the Admission and Placing (including professional fees, commissions, the costs of printing and the fees payable to the Registrars) are estimated to amount to approximately £0.7 million (excluding VAT).

19.2 Baker Tilly Corporate Finance LLP, whose registered office is at 6th Floor, 25 Farringdon Street, London EC4A 4AB, as reporting accountants, have given and not withdrawn their written consent to the inclusion of their report in Part III of this document in the form and context in which it is included.

19.3 HGF Limited, whose registered office is at Belgrave Hall, Belgrave Street, Leeds LS2 8DD, as patent and trade mark attorneys, have given and not withdrawn their written consent to the inclusion of their report in Part IV of this document in the form and context in which it is included and has authorised the contents of their report for the purposes of the AIM Rules. HGF Limited confirm that, having taken all reasonable care to ensure that such is the case, the information contained in Part IV of this document is, to the best of their knowledge, in accordance with the facts and contains no omission likely to affect its import.

19.4 PharmaVentures Limited, whose registered office is at 1300 Parkway Court, John Smith Drive, Oxford OX4 2JY, as an independent expert, have given and not withdrawn their written consent to the inclusion of their report in Part V of this document in the form and context in which it is included and has authorised the contents of their report for the purposes of the AIM Rules. PharmaVentures Limited confirm that, having taken all reasonable care to ensure

that such is the case, the information contained in Part V of this document is, to the best of their knowledge, in accordance with the facts and contains no omission likely to affect its import.

19.5 The auditors of the Company are Baker Tilly UK Audit LLP, whose registered office is at 6th Floor, 25 Farringdon Street, London EC4A 4AB, who were appointed on 21 November 2014. Prior to that date, the Company and Evgen were below the statutory threshold for an audit and had not appointed auditors.

19.6 Northland Capital, whose registered office is at 131 Finsbury Pavement, London EC2A 1NT, has given and not withdrawn its consent to the inclusion in this document of the references to its name in the form and context in which they are included.

19.7 Save as disclosed in this document, the Directors are not aware of any patents or intellectual property rights, licences or industrial, commercial or financial contracts or new technological processes which may be of material importance to the Company's business or profitability.

19.8 Save as disclosed in this document, there has been no significant change in the trading or financial position of (1) the Group since 31 March 2015, the date to which the Historical Financial Information disclosed in Part III of this document has been prepared and (2) the Company since 2 October 2014, being the date of its incorporation.

19.9 Save as set out in this document, no person (other than a professional adviser referred to in this document or trade supplier) has:

19.9.1 received directly or indirectly, from the Company within the 12 months preceding the Company's application for Admission; or

19.9.2 entered into contractual arrangements (not otherwise disclosed in this document) to receive directly or indirectly, from the Company on or after Admission any of the following:

(a) fees totalling £10,000 or more;

(b) securities in the Company with a value of £10,000 or more calculated by reference to the issue price; or

(c) any other benefit with a value of £10,000 or more at the date of Admission.

19.10 Save as disclosed in this document, since the period of the Historical Financial Information set out in Part III of this document, the Company has made no investments and there are no investments in progress which are or may be significant.

19.11 The Company's accounting reference date is 31 March.

19.12 Save as disclosed in this document, the Company is not aware of any arrangements which may at a subsequent date result in a change of control of the Company.

19.13 Save as disclosed in this document, there are no provisions in the Articles which would have the effect of delaying, deferring or preventing a change of control of the Company.

19.14 Save as disclosed in this document, no public takeover bids have been made by third parties in respect of the Company's issued share capital since its incorporation up to the date of this document.

19.15 Insofar as the Directors are aware, the percentage of Ordinary Shares not in public hands (as that expression is defined in the AIM Rules) on Admission is expected to be approximately 64 per cent.

19.16 Save as disclosed in this document, there are not, either in respect of the Company or its subsidiaries, any known trends, uncertainties, demands, commitments or events that are reasonably likely to have a material effect on the Company's prospects for at least the current financial year.

19.17 Save as disclosed in this document, there are no mandatory takeover bids and/or squeeze out and sell-out rules in relation to the Ordinary Shares.

19.18 Save as set out in this document, as far as the Directors are aware, there are no environmental issues that may affect the Company's utilisation of its tangible fixed assets.

19.19 Save as disclosed in this document, the Directors are unaware of any exceptional factors which have influenced the Company's recent activities.

19.20 The Directors are not aware of any other information that they should reasonably consider as necessary for the investors to form a full understanding of (i) the assets and liabilities, financial position, profits and losses, and prospects of the Company and the securities for which Admission is being sought; (ii) the rights attached to those securities; and (iii) any other matter contained herein.

19.21 The Placing will result in the allotment and issue of 18,918,919 New Ordinary Shares, diluting holders of Existing Ordinary Shares by 26 per cent.

20. THIRD PARTY INFORMATION

Where information has been sourced from a third party, the information has been accurately reproduced and, as far as the Company and the Directors are aware and are able to ascertain from information published by that third party, no facts have been omitted which would render the reproduced information inaccurate or misleading. Reference materials include various historical and recent publications. A comprehensive list of reports and information used in the preparation of this document is available if required.

21. AVAILABILITY OF ADMISSION DOCUMENT

A copy of this document is available free of charge from the registered office of the Company, and at the offices of Pinsent Masons LLP at 30 Crown Place, Earl Street, London EC2A 4ES, during normal business hours on any weekday (public holidays excepted) from the date of this document until at least one month after the date of Admission.

A copy of this document is also available on the Company's website, www.evgen.com

Dated: 15 October 2015

DEFINITIONS

The following definitions apply throughout this document unless the context requires otherwise:

''2008 Scheme''	has the meaning ascribed to that term in paragraph 12.1 of Part VI of this document
''2011 Plan''	has the meaning ascribed to that term in paragraph 12.1 of Part VI of this document
''2013 Loan Note Instrument''	has the meaning ascribed to that term in paragraph 10.13 of Part VI of this document
''2013 Notes''	has the meaning ascribed to that term in paragraph 10.13 of Part VI of this document
''2014 Loan Note Instrument''	has the meaning ascribed to that term in paragraph 10.16 of Part VI of this document
''2014 Notes''	has the meaning ascribed to that term in paragraph 10.16 of Part VI of this document
''A Shares''	the A ordinary shares of £0.0025 each in the capital of the Company in issue as at the date of this document
''Acceleris''	Acceleris Capital Limited
''Act''	the Companies Act 2006, as amended
''Admission''	admission of the Existing Ordinary Shares and the New Ordinary Shares to trading on AIM becoming effective in accordance with the AIM Rules for Companies
''AIM''	AIM, a market operated by the London Stock Exchange
''AIM Rules''	The AIM Rules for Companies and the AIM Rules for Nominated Advisers
''AIM Rules for Companies''	the rules for companies whose securities are admitted to trading on AIM, as published by the London Stock Exchange from time to time
''AIM Rules for Nominated Advisers''	the rules setting out the eligibility, ongoing obligations and certain disciplinary matters in relation to nominated advisers, as published by the London Stock Exchange from time to time
''Articles''	the articles of association of the Company as at the date of Admission, a summary of which is set out in paragraph 5 of Part VI of this document
''Audit Committee''	means the audit committee of the Board
''B Shares''	the B ordinary shares of £0.0025 each in the capital of the Company in issue as at the date of this document
''Board'' or **''Directors''**	the board of directors of the Company currently comprising the persons whose names are set out on page 5 of this document
''Clarat''	Clarat Partners LLP
''Company'' or **''Evgen Pharma''**	Evgen Pharma plc (registered number 09246681) of Liverpool Science Park Innovation Centre 2, 146 Brownlow Hill, Liverpool, Merseyside L3 5RF
''Company Options''	has the meaning ascribed to that term in paragraph 12.1 of Part VI of this document
''CREST''	the relevant system (as defined in the CREST Regulations) for paperless settlement of share transfers and the holding of shares in uncertificated form which is administered by Euroclear UK & Ireland Limited
''CREST Regulations''	the Uncertificated Securities Regulations 2001 (SI 2001/3755), as amended
''DBP''	means the Evgen Pharma Deferred Bonus Plan

''Disclosure and Transparency Rules''	the disclosure rules and transparency rules issued by the FCA, acting in its capacity as the competent authority for the purposes of Part VI of FSMA
''EIS''	the Enterprise Investment Scheme, as particularised in Part 5 of the Income Taxes Act 2007
''Enlarged Share Capital''	the total issued share capital of the Company immediately following Admission
''EU''	the European Union
''EV Group''	Enterprise Ventures Limited
''Evgen''	Evgen Limited (registered number 06403643) of Liverpool Science Park Innovation Centre 2, 146 Brownlow Hill, Liverpool, Merseyside L3 5RF, a wholly owned subsidiary of the Company
''Evgen Options''	has the meaning ascribed to that term in paragraph 12.1 of Part VI of this document
''Existing Articles''	the articles of association of the Company in force as at the date of this document
''Existing Ordinary Shares''	the 53,951,943 Ordinary Shares in issue immediately prior to Admission
''FCA''	the Financial Conduct Authority
''FSMA''	the Financial Services and Markets Act 2000, as amended
''Group''	the Company and its subsidiaries from time to time
''HGF''	HGF Limited
''HMRC''	HM Revenue & Customs
''Imprimatur Capital''	Imprimatur Capital Limited
''Investment Agreement''	the investment agreement dated 25 August 2011 between RSGF II, NWFB, Andrew Geoffrey Smithson, Ashcourt Rowan Pension Trustees Limited, Stephen Joseph Franklin, Evgen, Letzone Limited, South Yorkshire Investment Fund Limited, Alex Merolli, Barry Clare and Clarat as amended from time to time and as acceded to by the Company on 5 December 2014
''IPO''	initial public offering
''Loan Notes''	the 2013 Notes and 2014 Notes
''London Stock Exchange''	London Stock Exchange plc
''LTIP''	means the Evgen Pharma Long Term Incentive Plan
''LTIP IPO Awards''	has the meaning ascribed to that term in paragraph 12.5.4 of Part VI of this document
''New Ordinary Shares'' or **''Placing Shares''**	the 18,918,919 new Ordinary Shares to be issued by the Company and placed with Placees
''Northland Capital''	Northland Capital Partners Limited, nominated adviser and broker to the Company
''NWFB''	NWF (BIOMEDICAL) LP
''Official List''	the Official List of the UK Listing Authority
''Ordinary Shares''	ordinary shares of £0.0025 each in the capital of the Company
''Panel''	The Panel on Takeovers and Mergers
''PharmAgra''	PharmAgra Labs Inc.
''Placees''	subscribers for New Ordinary Shares procured by Northland Capital on behalf of the Company pursuant to the Placing Agreement

''Placing''	the arrangements for the procurement of subscribers for the New Ordinary Shares by Northland Capital (as agent for the Company pursuant to and on the terms of the Placing Agreement)
''Placing Agreement''	has the meaning ascribed to that term in paragraph 10.5 of Part VI of this document
''Placing Price''	37p for each New Ordinary Share
''Pre-IPO Round''	means the placing of 9,569 ordinary shares of £2.00 to subscribers procured by Acceleris at £209 per share which was completed on 26 August 2015
''Prospectus Rules''	the Prospectus Rules of the FCA brought into effect on 1 July 2005 pursuant to Commission Regulation (EC) No. 809/2004 and the Prospectus Regulations 2005 (SI 2005/1433)
''QCA''	Quoted Companies Alliance
''QCA Code''	the QCA Corporate Governance Code for Small and Mid-Sized Quoted Companies, including AIM Companies, as amended from time to time
''Registrar''	SLC Registrars, a division of Equiniti David Venus Limited
''Remuneration Committee''	means the remuneration committee of the Board
''RSGF II''	RisingStars Growth Fund II LP
''Sarum Capital''	Sarum Investment SICAV plc
''Shareholder(s)''	(a) person(s) who is/are registered as holder(s) of Ordinary Shares from time to time
''Standalone Unapproved Agreements''	has the meaning ascribed to that term in paragraph 12.1 of Part VI of this document
''subsidiaries''	any subsidiary as defined in the Act
''SYSCF''	South Yorkshire Investment Fund Limited (registered number 03936065) of 2nd Floor, Capitol Court, Dodworth, Barnsley S75 3TZ
''Takeover Code''	The City Code on Takeovers and Mergers
''UK'' or **''United Kingdom''**	United Kingdom of Great Britain and Northern Ireland
''USA'' or **''US''**	the United States of America
''US$''	US dollars
''uncertificated'' or **''in uncertificated form''**	recorded on the register of Ordinary Shares as being held in uncertificated form in CREST, entitlement to which, by virtue of the CREST Regulations, may be transferred by means of CREST
''VCT''	Venture Capital Trust, as particularised in Part 6 of the Income Taxes Act 2007
''Walker Crips''	Walker Crips Stockbrokers Limited
''Warrants''	has the meaning ascribed to that term in paragraph 10.8 of Part VI of this document
''£'' or **''Sterling''**	UK pounds Sterling

GLOSSARY

The following glossary terms apply throughout this document unless the context requires otherwise:

''α-cyclodextrin''	a polysaccharide ring of six glucose units that are covalently attached end to end. It is a source of dietary fibre marketed for a range of medical, healthcare and food applications
''API''	active pharmaceutical ingredient
''aromatase inhibitor''	class of drugs used in the treatment of breast cancer and ovarian cancer in postmenopausal women. Aromatase is the enzyme that synthesizes eostrogen
''bioavailability''	the fraction of an administered dose of unchanged drug that reaches the systemic circulation, one of the principal pharmacokinetic properties of drugs. By definition, when a medication is administered intravenously, its bioavailability is 100 per cent.
''Biozzi ABH CREAE''	an inbred strain of mice susceptible to the development of experimental allergic encephalomyelitis (EAE) following injection of spinal cord homogenate in adjuvant. The mice develop a chronic relapsing pattern of disease characterised by mononuclear infiltration of the central nervous system, with demyelination being particularly evident in relapse.
''calcium channel blocker''	a class of medications that disrupts the movement of calcium through calcium channels which are typically used as antihypertensive drugs, i.e. as medications to decrease blood pressure in patients with hypertension
''cancer stem cells''or **''CSCs''**	cancer cells (found within solid tumours or haematological cancers) that possess characteristics associated with normal stem cells, specifically the ability to give rise to all cell types found in a particular cancer sample
''cGMP''	Current Good Manufacturing Practice. The process of controlling the quality of drug products by carefully monitoring drug manufacturers' compliance as monitored by regulatory bodies such as the FDA
''COPD''	Chronic Obstructive Pulmonary Disease: a type of obstructive lung disease characterised by chronically poor airflow
''CRO''	Contract Research Organisation
''CSIC''	Consejo Superior de Investigaciones Científicas
''delayed cerebral ischaemia''	delayed cerebral ischaemia (or symptomatic vasospasm) refers to a condition in which a blood vessel's spasm leads to vasoconstriction. leading to tissue ischaemia and tissue death (necrosis)
''dimethyl fumerate''	the methyl ester of fumaric acid. First licensed in Germany as oral therapy for psoriasis and more recently licensed under the brand Tecfidera as an oral therapy for RR-MS
''EAE''	experimental autoimmune encephalomyelitis, sometimes referred to as experimental allergic encephalomyelitis, is an animal model of brain inflammation. It is an inflammatory demyelinating disease of the central nervous system (CNS). It is mostly used with rodents and is widely studied as an animal model of the human CNS demyelinating diseases, including multiple sclerosis and acute disseminated encephalomyelitis (ADEM)
''endocrine therapy''	manipulation of the endocrine system through exogenous administration of specific hormones, particularly steroid hormones, or drugs which inhibit the production or activity of such hormones (hormone antagonists)

''ER+ / ER–''	endocrine receptor (estrogen or progesterone receptor) positive is a breast cancer subtype that grows in response to estrogen or progesterone. In contrast, ER negative are unresponsive to the same hormones
''FDA''	the Food and Drug Administration is a federal agency of the United States Department of Health and Human Services, one of the United States' federal executive departments
''GI''	gastrointestinal
''GMP''	Good Manufacturing Practice is a term that is recognised worldwide for the control and management of manufacturing and quality control testing of pharmaceutical products
''GRAS''	FDA designation that a chemical or substance added to food is considered safe by experts, and so is exempt from some regulation
''HDAC''	DNA is wrapped around histones. Histone deacetylases (HDAC) are a class of enzymes that allow the histones to wrap the DNA more tightly thereby regulating DNA expression
''HER+''	HER+ cancer cells make too much of a protein known as HER2/ neu. These breast cancers tend to be much more aggressive and fast-growing
''ICH''	International Conference on Harmonisation, an internationally harmonised standard of technical requirements for registration of pharmaceuticals for human use
''indication''	in medicine, an indication is a valid reason to use a certain test, medication, procedure, or surgery. The opposite of indication is contraindication
''intracerebral haemorrhage''	a haemorrhage that occurs when a diseased blood vessel within the brain bursts, allowing blood to leak inside the brain
''in vitro''	studies performed with cells or biological molecules studied outside their normal biological context
''in vivo''	studies performed on whole, living organisms usually animals including humans
''IP''	means all patents, rights to inventions, copyright and related rights, moral rights, database rights, supplementary protection certificates, petty patents, utility models, rights in designs, trade marks, service marks, trade names, domain names, rights in goodwill or to sue for passing-off, rights in unfair competition, rights in undisclosed or confidential information (such as know how, trade secrets and inventions (whether patentable or not)) and other similar or equivalent rights or forms of protection (whether registered or unregistered) and all applications (or rights to apply) for, and for renewals and extensions of, such rights as may now or in the future exist anywhere in the world
''MHRA''	the Medicines and Healthcare Products Regulatory Agency is responsible for regulating all medicines and medical devices in the UK by ensuring they work and are acceptably safe
''metastatic''	metastasis, or metastatic disease, is the spread of a cancer or disease from one organ or part to another not directly connected with it
''MOG35-55 C57BL6''	a model of EAE induced in C57 black 6 mice by immunisation with the amino acid sequense from 35-55 from myelin oligodendrocyte glycoprotein

''mTORC-1''	also known as mammalian target of rapamycin complex 1 or mechanistic target of rapamycin complex 1, is a protein complex that functions as a nutrient/energy/redox sensor and controls protein synthesis
''multiple sclerosis (MS)''	an inflammatory disease in which the insulating covers of nerve cells in the brain and spinal cord are damaged
''NF-kB''	nuclear factor kappa-light-chain-enhancer of activated B cells is a protein complex that controls transcription of DNA. NF-κB is found in almost all animal cell types and is involved in cellular responses to stimuli such as stress. NF-κB can be understood to be a protein responsible for cytokine production and cell survival
''nimodipine''	a type of calcium channel blocker used to reduce the major complication of subarachnoid haemorrhage, termed vasospasm
''Nrf2''	nuclear factor (erythroid-derived 2)-like 2, also known as NFE2L2 or Nrf2, is a transcription factor that in humans is encoded by the *NFE2L2* gene. Nrf2 regulates the expression of antioxidant proteins that protect against oxidative damage triggered by injury and inflammation
''orphan drug''	an orphan drug is a pharmaceutical agent that has been developed specifically to treat a rare medical condition, the condition itself being referred to as an orphan disease and the acknowledgement of that status by the regulatory authority referred to as the orphan designation
''oxidative stress''	oxidative stress reflects an imbalance between the systemic manifestation of reactive oxygen species and a biological system's ability to readily detoxify the reactive intermediates or to repair the resulting damage
''PSA''	Prostate-Specific Antigen, a biomarker associated with prostate cancer
''pharmacokinetics''	the study of how the body affects a specific drug after administration through the mechanisms of absorption and distribution, as well as the chemical changes of the substance in the body
''Phase I trial''	testing of a drug in patients or healthy volunteers to show that it is safe for a small group of people and to find the best dose and schedule for future research of the drug or drug combination
''Phase II trial''	testing of a drug in patients to provide more information about the safety of the new treatment and how well it works to treat a specific disease
''Phase IIa''	pilot clinical trials to evaluate efficacy (and safety) in selected populations of patients with the disease or condition to be treated, diagnosed, or prevented. Objectives may focus on dose-response, type of patient, frequency of dosing, or numerous other characteristics of safety and efficacy.
''Phase IIb''	well controlled trials to evaluate efficacy (and safety) in patients with the disease or condition to be treated, diagnosed, or prevented. These clinical trials usually represent the most rigorous demonstration of a medicine's efficacy. Sometimes referred to as pivotal trials
''relapsing-remitting multiple sclerosis''	characterised by attacks or flare-ups during which new symptoms appear or old symptoms worsen; they may be mild or severe but all may leave lasting damage to the nerves
''reproductive toxicology studies''	testing of potential adverse effects on sexual function and fertility in adult males and females, as well as developmental toxicity in the offspring

''subarachnoid haemorrhage'' or **''(SAH)''**	bleeding into the subarachnoid space, the outer cavity of the brain
''sulforaphane''	a molecule within the isothiocyanate group of organosulfur compounds and produced in some cruciferous vegetables when the enzyme, myrosinase, hydrolyses its precursor, glucoraphanin
''tamoxifen''	the usual endocrine (anti-estrogen) therapy for hormone receptor-positive breast cancer in pre-menopausal women
''topically applied''	applied to body surfaces such as the skin or mucous membranes to treat ailments
''traumatic brain injury'' or **''TBI''**	also known as intracranial injury, occurs when an external force traumatically injures the brain
''triple negative breast cancer''	refers to any breast cancer that does not express the genes for estrogen receptor (ER), progesterone receptor (PR) and Her2/neu
''Wnt/beta-catenin pathway''	a signal transduction pathway that regulates cell fate decisions during development
''xenograft''	the transplantation of living cells, tissues or organs from one species to another. Such cells, tissues or organs are called xenografts