THIS DOCUMENT IS IMPORTANT AND REQUIRES YOUR IMMEDIATE ATTENTION. If you are in any doubt about the contents of this document and the action you should take, you are recommended immediately to seek your own advice from a person duly authorised under the Financial Services and Markets Act 2000 who specialises in the acquisition of shares and other securities.

The Directors of Physiomics plc, whose names appear on page 4 of this document, accept responsibility both individually and collectively for the information contained in this document. To the best of the knowledge of the Directors (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 makes no omission likely to affect the import of such information.

Application has been made for the admission of the entire issued and to be issued share capital of the Company to trading on the AIM market of London Stock Exchange plc ("AIM"). It is expected that dealings in the Ordinary Shares will commence on AIM on 20 December 2004.

The rules of AIM are less demanding than those of the Official List of the UK Listing Authority. AIM is a market designed primarily for emerging or smaller companies to which a higher investment risk tends to be attached than to larger or more established companies. AIM securities are not admitted to the Official List of the United Kingdom Listing Authority.

A prospective investor should be aware of the risks of investing in such companies and should make the decision to invest only after careful consideration and, if appropriate, consultation with an independent financial adviser.

Neither the UK Listing Authority nor the London Stock Exchange plc has examined or approved the contents of this document. It is emphasised that no application is being made for admission of these securities to the Official List of the UK Listing Authority. The Ordinary Shares are not dealt on any other recognised investment exchange and no application has been or is being made for the Ordinary Shares to be admitted to any such exchange.

This document constitutes an AIM admission document drawn up in accordance with the AIM Rules and does not comprise a prospectus under the Public Offers of Securities Regulations 1995 (as amended). A copy of this document has not been delivered to the Registrar of Companies in England and Wales.

# **Physiomics plc**

(Incorporated in England and Wales under the Companies Act 1985 with registered number 4225086)

Placing of 37,500,000 Ordinary Shares of 0.04p at a price of 2p per Ordinary Share

and

Admission to trading on AIM

Nominated Adviser	Broker
Grant Thornton Corporate Finance	HB-corporate

Share capital immediately following the Placing				
A	luthorised		Issued a	nd Fully Paid
Number	Nominal Amount		Number	Nominal Amount
25,000,000,000	£10,000,000	Ordinary Shares of 0.04p each	230,025,599	92,010

Grant Thornton Corporate Finance, a division of Grant Thornton UK LLP, which is authorised and regulated by the Financial Services Authority, is the Company's nominated adviser for the purposes of the AIM Rules and as such, its responsibilities are owed solely to the London Stock Exchange plc and are not owed to the Company or any director or any other entity or person. Grant Thornton Corporate Finance will not be responsible to anyone other than the Company for providing the protections afforded to clients of Grant Thornton Corporate Finance or for advising any other person in connection with the Placing and Admission.

HB-corporate, a trading division of Hoodless Brennan & Partners Plc, which is authorised and regulated by the Financial Services Authority, and which is a member of London Stock Exchange plc is acting as broker to the Company and no one else. HB-corporate will not be responsible to anyone other than the Company for providing the protections afforded to clients of HB-corporate or for providing advice in relation to the Placing and Admission.

The Ordinary Shares have not been, nor will they be, registered under the US Securities Act of 1933 or under any applicable securities laws of Canada, Australia, the Republic of South Africa, the Republic of Ireland or Japan. The Ordinary Shares may not be offered or sold or delivered, directly or indirectly, in or into the United States, Canada, Australia, the Republic of South Africa, the Republic of Ireland or Japan. This document must not be mailed or otherwise distributed or sent to or into the United States, Canada, Australia, the Republic of South Africa, the Republic of Ireland or Japan. This document does not constitute an offer for, or the solicitation of an offer to subscribe for or by, any of the Ordinary Shares to any person in any jurisdiction to whom it is unlawful to make such an offer or solicitation in such jurisdiction.

Prospective investors should read the whole text and contents of this document and should be aware that an investment in the Company is speculative and involves a degree of risk. In particular, prospective investors' attention is drawn to the section entitled "Risk Factors" in Part III of this document.

#### FORWARD-LOOKING STATEMENTS

This document contains forward-looking statements. These statements relate to the Group's future prospects, developments and business strategies.

Forward-looking statements are identified by their use of terms and phrases such as "believe", "could", "envisage", "estimate", "intend", "may", "plan", "will" or the negative of those, variations or comparable expressions, including references to assumptions. These statements are primarily contained in Parts I and II of this document.

The forward-looking statements in this document are based on current expectations and are subject to risks and uncertainties that could cause actual results to differ materially from those expressed or implied by those statements.

Certain risks to and uncertainties of the Group are specifically described in Part III of this document headed "Risk Factors". If one or more of these risks or uncertainties materialises, or if underlying assumptions prove incorrect, the Group's actual results may vary materially from those expected, estimated or projected. Given these risks and uncertainties, potential investors should not place any reliance on forward-looking statements.

These forward-looking statements speak only as at the date of this document. Neither the Directors nor the Company undertake any obligation to update forward-looking statements or risk factors other than as required by the AIM Rules or by the rules of any other securities regulatory authority, whether as a result of new information, future events or otherwise.

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# DIRECTORS, SECRETARY AND ADVISERS

Directors	Dr Stephen Barry Parker, <i>Non-executive Chairman</i> Dr John Savin, <i>Chief Executive Officer</i> David Alford Collins, <i>Finance Director</i> Professor David Andrew Fell, <i>Non-executive Science Director</i> Dr Paul Bernard Harper, <i>Non-executive Director</i> John Kingston Pool, <i>Non-executive Director</i>
	All of: The Magdalen Centre Oxford Science Park Robert Robinson Avenue Oxford OX4 4GA
Company Secretary and Registered Office	David Alford Collins The Magdalen Centre Oxford Science Park Robert Robinson Avenue Oxford OX4 4GA
Nominated Adviser	Grant Thornton Corporate Finance Grant Thornton House Melton Street Euston Square London NW1 2EP
Broker to the Company	HB-corporate 40 Marsh Wall London E14 9TP
Solicitors to the Company	Bircham Dyson Bell 50 Broadway Westminster London SW1H 0BL
Solicitors to the Placing	Rosenblatt Solicitors 9-13 St Andrew Street London EC4A 3AF
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Reporting Accountants	Grant Thornton UK LLP 1-4 Atholl Crescent Edinburgh EH3 8LQ
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Registrars	Capita Registrars The Registry 34 Beckenham Road Beckenham Kent BR3 4TU

### **KEY INFORMATION**

The following information should be read in conjunction with the full text of this document, from which it is derived. You are advised to read this document in its entirety and not just rely on the key information below, before making a decision as to whether or not to invest in Ordinary Shares. In particular, your attention is drawn to the risk factors set out in Part III of this document.

### Business

The business of Physiomics is the development and sale of services aimed at reducing the high cost of drug development for pharmaceutical and biotechnology companies, principally by optimising the design of their clinical trials through the application of computer-based simulation tools. The services have a particular focus on cancer therapies.

Industry drug development costs average \$800 million per product, reflecting failure rates of between 80 to 90 per cent. mainly at the early clinical trial stage. Improving overall success rates by 10 per cent. could save the industry US\$242 million per drug.

The Company is also applying its technologies to develop proprietary cancer therapy products for outlicensing and to this end has secured an option to license up to two innovative molecules from a drug development company.

# Services

The Company's services apply complex computer-based simulation tools to resolve the two main problems associated with drug development, namely (i) the lack of a biological response to a given dose and (ii) the difficulties involved in determining the adequate dose of a drug.

These services combine the Company's own patented pharmacodynamic ("PD") technology (which enables the correct drug dose at the disease site to be predicted at an early stage) with the Bayer Technology Services GmbH's pharmacokinetic ("PK") technology (which is used to evaluate how much drug is needed at the target site to achieve therapeutic levels). They represent an innovative collaboration which is designed to satisfy the growing demand for simulation technologies which streamline drug development from the preclinical phase through to Phase III.

The Directors believe that drug companies will use Physiomics' services to achieve a number of different objectives, for example:

- designing the clinical trial, to maximise the chances of a successful outcome; or
- troubleshooting problem trials, in order to identify the remedial action required and salvage drug development programmes; or
- evaluating the benefits of buying in, or outlicensing, potential drug development projects.

# Market opportunity

The market for systems biology products and services is expected to grow to \$785 million by 2008, an annual compound growth rate of 66 per cent. Despite the potential size of the market, the Directors believe that the level of complexity involved in simulation tools constitutes such a major barrier to entry that most pharmaceutical and biotechnology companies will outsource rather than develop their own simulation technology.

Physiomics and Bayer Technology Services ("BTS") are collaborating to market their integrated services globally to pharmaceutical and biotechnology companies. Services are targeted at companies with cancer products either about to enter human clinical testing or in the first stages of the clinical development process. These are the high risk stages with escalating investment costs. The two companies have also agreed to co-develop the next generation of technology. They are already in negotiations with a number of actual or potential clients.

# Marketing strategy

The Company is applying the considerable experience and range of contacts of its Directors to developing its customer base. This will supplement the access it already has to a range of industry data sources which enables it to identify all current public drug development projects. In addition, it has retained the services of a highly experienced business development consultant to assist in securing contracts.

# Competition

Physiomics' collaboration with BTS is the platform for the integration of the PK and PD aspects of cancer clinical development, both of which the Directors believe are crucial to customer success. This integration does not appear to be matched by any other supplier. Further, the Directors believe that Physiomics has an additional competitive advantage through its ownership of its SystemCell<sup>TM</sup> technology (for creating diverse cell populations where each cell encapsulates its own copy of the simulation) over which a US patent has been granted. As the Company accumulates a larger number of integrated and validated modules, the value of the simulation content becomes higher and the perceived utility to customers greater.

# **Background to the Placing**

The Company commenced trading in July 2001. In August 2002 it was acquired by EiRx Pharma for £7 million payable in shares of EiRx Pharma.

The Company is now undertaking the Placing to raise £750,000 before expenses which will be used to implement its marketing strategy, assist the development of its core services and to participate in proprietary therapeutic development projects.

# DEFINITIONS

The following definitions and terms	apply throughout this document unless the context otherwise requires:
"Act"	the Companies Act 1985 (as amended)
"Admission"	admission of the entire issued share capital of the Company (including the Placing Shares) to trading on AIM becoming effective in accordance with Rule 6 of the AIM Rules
"AIM"	the AIM Market of the London Stock Exchange
"AIM Rules"	the rules relating to AIM published by the London Stock Exchange
"BTS"	Bayer Technology Services GmbH, a company incorporated in Germany
"Combined Code"	the Principles of Good Governance and the Code of Best Practice included within the Listing Rules of the UKLA
the "Company" or "Physiomics"	Physiomics plc
"CREST"	the system of paperless settlement of trades and the holding of uncertificated shares of which CRESTCo Limited is the operator
"Cyclacel"	Cyclacel Limited, a company incorporated in England and Wales
"Directors" or "Board"	the directors of the Company being Stephen Parker, John Savin, David Fell, David Collins, Paul Harper and John Pool
''EiRx Pharma''	EiRx Pharma Limited, a private company incorporated in England and Wales with registered number 4447266, which is the parent company of the Company
"Enlarged Issued Share Capital"	the issued share capital of the Company as enlarged by the Placing and the Fee Shares
''e-phen''	e-phen Limited, a private company incorporated in England and Wales with registered number 3955773 and a wholly-owned subsidiary of the Company
"Fee Shares"	the Ordinary Shares allotted and issued to Billam AG and Billam plc under the terms of the Put and Call Option Agreement, further details of which are set out in paragraph 5 of Part V of this document
"Grant Thornton Corporate Finance"	the corporate finance division of Grant Thornton UK LLP which is authorised and regulated by the Financial Services Authority to carry on investment business
"Group"	the Company together with its subsidiary, e-phen, details of which are set out in paragraph 2 of Part V of this document
"HB-corporate"	a trading division of Hoodless Brennan & Partners Plc, which is authorised by the Financial Services Authority to carry on investment business
"London Stock Exchange"	London Stock Exchange plc
"Official List"	the Official List of the UKLA
"Ordinary Shares"	ordinary shares of 0.04p each in the capital of the Company
"PK-Sim""	PK-Sim <sup>®</sup> , a software system owned by BTS
"Placing Agreement"	the agreement between the Company, HB-corporate, EiRx Pharma and the Directors in connection with the Placing, details of which are set out in paragraph 5 of Part V of this document
"Placing"	the conditional placing of the Placing Shares at the Placing Price

"Placing Price"	2 pence per Ordinary Share
"Placing Shares"	37,500,000 Ordinary Shares to be allotted and issued pursuant to the Placing
"POS Regs"	The Public Offers of Securities Regulations 1995 (as amended)
"Shareholders"	holders of Ordinary Shares
"SystemCell <sup>TM</sup> "	SystemCell <sup>TM</sup> a patented technology of the Company further details of which are set out in Part I and Part II of this document
"UKLA"	the UK Listing Authority of the Financial Services Authority, acting in its capacity as the competent authority for the purposes of Part VI of the Financial Services and Markets Act 2000

# **GLOSSARY AND ABBREVIATIONS**

"absorption"	the transfer of compound across an external physiological barrier
"ADME"	the absorption, metabolism, distribution and excretion. A study of how and to what extent, a substance is taken up by the body and the substance's subsequent fate
"antisense"	in molecular biology, the strand complementary to a coding sequence of a nucleic acid
"antisense drugs"	drugs designed to emulate antisense RNA, which hybridizes with and inactivates mRNA. These drugs are short sequences of RNA that attach to mRNA and stop a particular gene from producing the protein for which it holds the recipe
"apoptosis"	a regulated series of events that occurs in cells and results in their death. Many cancer cells have lost the ability to trigger apoptosis and continue to grow and invade healthy tissue
"bioinformatics"	a science that evolved to analyse the gene and protein sequences from the many genome sequencing projects including the human genome
"cell"	the basic unit of any living organism containing the genes required to function. It is a small watery membrane-bound compartment filled with chemicals and a complete copy of the organism's genome. All living organisms are made of one or more cells
"chemotherapy"	the systemic treatment with drugs to kill cancer cells (tumours)
''clinical''	relating to, or conducted in, or as if in, the clinic
"combinatorial chemistry"	chemical techniques for producing large numbers of variants of basic drug-like compounds to generate a vast library of structures for use in high-throughput screening
"distribution"	the transfer of compound from the site of administration to the total systemic circulation and then to extracellular and intracellular water and tissues
''drug''	an agent that modulates a physiological state and that may be used to treat, diagnose, mitigate or prevent a disease
"drug Discovery"	the process of researching new substances that may become treatments for various human conditions
"enzyme"	proteins that catalyse (enable) and increase the speed of a biochemical transformation without altering the nature or direction of the reaction
"excretion"	the elimination of the bi-products of metabolism from the body, either via the urine, faeces, expired air or sweat
"GeneICE"	a therapeutic biological construction consisting of a specific single strand DNA sequence (giving gene specificity) linked to protein molecules that allow it to enter the nucleus and to recruit HDAC enzymes to suppress the specific gene function.
"gene"	the basic biological unit of heredity. A segment of deoxyribonucleic acid (DNA) needed to contribute to a function
"in silico"	within a computer model
"in vitro"	an experimental trial (involving biological matter) which is done in test tubes or petri dishes rather than within a living organism
"lead"	a molecule that interacts with a biological target and modulates its behaviour in a desirable way

"liposomes"	small synthetic fat vesicles designed to carry therapeutics to cells and to enable the therapeutic to enter the cells
''metabolism''	the universe of chemical changes occurring in a tissue. This consists of creating large molecules from smaller ones (anabolic changes) and small molecules from larger ones (catabolic changes)
"molecule"	the result of two or more atoms combining by chemical bonding: a molecule is the smallest physical unit of that particular substance
"mRNA"	messenger RNA; a nucleic acid that transmits genetic information from DNA to the cytoplasm where it is translated into protein which controls certain processes in the cell
''neoplasm''	an over growth of tissue. This can be referred to as benign or malignant
''nucleic acid''	a complex, high-molecular-weight biochemical macromolecule composed of chains that convey genetic information
"Phase I"	the first stage of human clinical testing of a new pharmaceutical usually conducted in healthy volunteers. Studies are designed to assess the absorption, distribution, metabolism and elimination of the test drug to permit selection of an optimal dosing regimen for clinical research
"Phase II"	therapeutic studies in small numbers of patients using data generated in Phase 1 studies to guide dosing regimens and to examine therapeutic outcomes and monitor for signs of toxicity
"Phase III"	pivotal studies where the drug candidate is tested in at least two large scale trials. The aim is to demonstrate a therapeutic index that is statistically better than placebo or the current best therapy
"pharmacodynamics"	the response of an organism (cell or patient) to a drug. It may require biochemical tests or recording of qualitative clinical symptoms
"pharmacokinetics"	the absorption, metabolism, distribution and excretion of pharmaceuticals in animal models and man
"pre-clinical"	prior to testing in humans
"protein"	large complex biological molecules that are essential to the structure, function and regulation of cells, organs and tissues
"Rational Therapy Design System"	a mathematical, systems biology simulation of the biochemical reactions regulating the growth and division of mammalian cells used to understand the action of anti-cancer drugs. By using SystemCell <sup>TM</sup> , many copies of this simulation can be run simultaneously
"RNA"	ribonucleic acid
"siRNA"	small interfering RNA, a technique used to prevent translation of specific genes by targeting and degrading its RNA
"systems biology"	the understanding of how proteins and genes, as components of an overall pathway and network, interact to generate biological function
"target"	a biological molecule, usually a protein, whose function can be modulated by a drug's action to affect a disease state
''toxicological''	poisonous or harmful
"tumour"	an abnormal mass of tissue also called a neoplasm, that is the result of uncontrolled cell division

# PLACING STATISTICS

Placing Price	2p
Number of existing Ordinary Shares	191,845,911
Number of Fee Shares	679,688
Number of Placing Shares	37,500,000
Number of Ordinary Shares on Admission (including Placing Shares and Fee Shares)	230,025,599
Placing Shares as a percentage of the Enlarged Issued Share Capital on Admission	16.3 per cent.
Market capitalisation of the Company following Admission at the Placing Price	£4.6 million

# EXPECTED TIMETABLE

Admission effective and dealings expected to commence on AIM	20 December 2004
CREST accounts credited	20 December 2004
Expected date of despatch of definitive share certificates for Ordinary Shares	29 December 2004

# PART I

# **INFORMATION ON THE COMPANY**

### 1. Introduction

### Industry background

Drug discovery is a lengthy and expensive process typically taking up to 12 years or more to complete. Average development costs of a drug, including the cost of failed drug candidates, are currently estimated to be \$800 million per product. The process is risky and unpredictable with approximately 80 to 90 per cent. of all clinical drug candidates failing to reach the market.

Independent analysis of pharmaceutical drug development shows that, if the success rates from Phase I to market could be increased by 10 per cent. overall, from its current level of 21 per cent. a net \$242 million per drug (30 per cent. of costs) could be saved. On this basis, in the 10 years to 2002, over 300 new drugs were approved by the US Food and Drug Authority and, as a consequence, the pharmaceutical industry could have potentially saved approximately \$75 billion during this period.

The Directors believe that *in silico* simulation technologies will quickly become the essential tools of the pharmaceutical industry as a means of reducing this attrition. They also believe that the level of complexity of such "systems biology" simulation tools constitutes a significant barrier to entry, a factor that will encourage industry participants to outsource rather than develop their own simulation technology.

Recent market research suggests that the market for systems biology products and services is expected to grow to \$785 million by 2008 at an annual compound growth rate of 66 per cent. The Directors believe that the worldwide market for pharmacokinetic software and services, including clinical trial design, is currently growing at 40 per cent. per annum.

# Physiomics' services

The two main aspects of pharmaceutical development addressed by simulation technologies are (i) problems due to lack of biological response to the dose (pharmacodynamics or "PD") and (ii) difficulties in administering an adequate dose of a drug (pharmacokinetics or "PK"):–

- PD problems frequently arise from poor or unpredictable biological responses usually as a result of the complexity and non-linear response mechanisms of biochemical pathways. To predict PD responses, sophisticated computer simulations are being developed by Physiomics and used to model the dynamics of complex biochemical pathways, including the simulation of cell division. Physiomics uses a variety of simulation tools to generate and solve sets of non-linear differential equations that describe how the biological components of the model are changing with time. Physiomics is presently conducting single cell simulations for clients. However, it is developing a multi-cellular model based on a patented technology, SystemCell<sup>TM</sup>, to create virtual biological cell populations, where each cell encapsulates its own copy of the simulation.
- PK problems result from either insufficient quantities of a drug reaching a given target or the toxic effects associated with the accumulation of excessive quantities of a drug.

Physiomics develops and sells simulation services and consultancy to pharmaceutical and biotechnology companies designed to reduce the cost of their research and drug development programs.

To address PK issues, Physiomics has entered into an agreement with BTS (part of the Bayer group) whereby Physiomics has been granted the right to use and market BTS's PK-Sim<sup>®</sup> software on a worldwide non-exclusive basis. PK-Sim<sup>®</sup> is one of a new generation of products used to assess the PK properties of a drug.

Physiomics, in collaboration with BTS, develops and sells an integrated suite of simulation services and products, comprising Physiomics' PD services and BTS's PK-Sim<sup>®</sup>, that is designed to satisfy the growing demand from the pharmaceutical and biotechnology industries for simulation technology to streamline drug discovery from the pre-clinical phase through to Phase III. The two companies have agreed to jointly market services and products and further to co-develop the next generation of the technology.

The Directors of Physiomics believe that the economic case for the use of an integrated simulation-led approach to drug development is clear. The Directors also believe that the Physiomics-BTS integration of PD and PK is innovative and presents Physiomics with an important route to market. The Directors believe that this collaboration has created a leading European position in the sector with only a few US-based

competitors. Physiomics and BTS are already in negotiations with a number of actual or potential clients to apply these products to clinical trial design.

# In-house drug development

The Company is also seeking opportunities to co-fund its own, or take a share in other drug development projects using PD and PK technologies. In this way the Directors believe they will be able to leverage additional milestones and royalty payments from projects and deliver significant value to Shareholders. To this end, Physiomics has also secured an option to license up to two innovative molecules from Cronos Therapeutics Limited, which it intends to evaluate for the potential development of proprietary products for cancer therapy.

Further information about Physiomics' products, markets and technology is described in Part II of this document.

# Physiomics' marketing approach

Physiomics, in collaboration with BTS, is offering a range of services aimed at optimising or troubleshooting clinical trials, typically requiring the use of both PK-Sim<sup>®</sup> and the sophisticated modelling supplied by Physiomics. Clients will typically be pharmaceutical or biotechnology companies seeking to steamline their clinical trials process.

Physiomics is applying the considerable experience and range of contacts of its Directors to developing its customer base. In addition to the industry knowledge of its management team, Physiomics has a range of industry data sources including the comprehensive, online PharmaProjects database. This enables all current public pharmaceutical development projects to be identified giving precision targeting for business development and sales investment.

The collaboration with BTS is expected itself to provide an important additional global sales channel for Physiomics' services. Most projects are likely to be sold and run jointly under a profit sharing arrangement. Physiomics and BTS have already carried out joint sales training and undertake combined sales and marketing activities.

Physiomics has retained a highly experienced business development consultant, Gavin Clarke, to assist in securing contracts with major US or European pharmaceutical or biotechnology companies with a late preclinical or Phase I/Phase II cancer project. The proposed model is to run focused, integrated systems biology simulations alongside the standard development path for a customer's project to enable the customer to optimise the design of further clinical trials. In this scenario, both Physiomics and BTS's expertise would be required. The Company is also seeking to provide services to mid range pharmaceutical and biotechnology companies. Experience indicates that typical projects will initially be for PK work that could extend into systems biology projects as clinical development progresses.

# Physiomics' competitive position

Physiomics competes through being highly focused on applying cancer systems biology to clinical trial design. The collaboration with BTS enables integration of the PK and PD aspects of clinical development both of which the Directors believe are crucial to customer success. This integration does not appear to be matched by any other supplier. In addition, the SystemCell<sup>TM</sup> technology for creating diverse cell populations is covered by a granted US patent owned by Physiomics. The Directors believe this will be a major barrier to the use of other simulations in the high-value US clinical market. In addition, the complexities of systems biology itself are a barrier to entry both for competitors and also for in-house development efforts in major companies. As Physiomics accumulates a larger number of integrated and validated biology modules, the value of the simulation content becomes higher and the perceived utility to customers greater.

# Intellectual property

Several patents, based on an international application (PCT/GB1996/002703) and entitled "Process Control", cover core technology used in the SystemCell<sup>TM</sup> software ("the Software"). The Patent Co-operation Treaty ("PCT") application was filed on 5 November 1996.

US Patent 6,446,055 was granted on 3 September 2002 and assigned to Physiomics on 14 November 2002. This assignment has been duly recorded at the US Patent and Trademark Office. The corresponding European patent 0 937 286 has been granted in the UK, Ireland, France, Germany, Holland, Italy and Sweden. The patent was assigned on 27 August 2002 to Physiomics, but the assignment has not yet been

recorded at the various national patent offices. Registration of the assignment will be undertaken as soon as practicable. The same assignment transfers copyright in the Software to Physiomics, and also contains a licence back enabling the grantee to use the Software for certain entertainment purposes.

# 2. History of the Company

Physiomics was founded by Peter Hoskins in May 2001. On 26 July 2001 Physiomics acquired e-phen, a company that had an option to license over the life science applications of a novel, patented autonomous object orientated software technology. Following the acquisition of e-phen, Dr John Savin, a director of e-phen, and Professor David Fell were appointed Directors of the Company. The licence option was exercised immediately following the acquisition and the Company commenced trading the same month.

On 1 August 2002, Physiomics was acquired by EiRx Pharma for £7 million payable by the issue of shares in EiRx Pharma.

In September 2002, Cyclacel Limited, a cancer drug development company based in Scotland, engaged Physiomics to work on a cell cycle simulation for use in assessing anti-cancer therapies. This work is ongoing. A joint scientific presentation was made at an international conference of systems biology in October 2004 at which some of the results of this work were presented.

On 1 October 2002, Physiomics commenced work part-funded by a DTI SMART feasibility award to develop a Rational Therapy Design System. The resulting model has been successfully tested against published laboratory data. Further laboratory validation and collection of relevant data for the model is being obtained through a collaboration with the University of Barcelona.

On 20 July 2004, Physiomics entered into a technology and marketing agreement with BTS. This collaboration enables Physiomics to link simulations of pharmacokinetics developed by BTS to models of cancer response from its Rational Therapy Design System.

On 11 August 2004, Physiomics entered into an agreement with Cronos Therapeutics Limited for an option to evaluate and license that company's GeneICE therapeutic technology in cancer. The two companies also agreed to co-develop any therapeutic products in the area of cancer that might result from the collaboration.

Between the commencement of trading in July 2001 and 30 September 2004, the Company received funding of approximately £0.75 million from World Life Sciences plc, Urco Limited, Billam plc, Billam AG, Peter Hoskins and a number of private investors.

Since July 2001, the Company has also received consultancy and other services from Peter Hoskins, Billam AG and John Pool. These fees, together with fees incurred after 30 June 2004, have been satisfied by the issue of shares, details of which are set out in paragraph 11(d) of Part V of this document.

# 3. Current trading and prospects

In addition to the agreements with BTS, Cyclacel and Cronos Therapeutics Limited, a number of other contracts and collaborations are currently being discussed and negotiated.

Since 30 June 2004 the Company has continued to incur development expenditure.

The Company is undertaking the Placing in order to raise funds to implement its marketing strategy, to assist the development of its core services and to participate in proprietary therapeutic development projects.

# 4. Details of the Placing

On behalf of the Company, HB-corporate has, under the terms of the Placing Agreement, conditionally placed with institutional and other investors a total of 37,500,000 new Ordinary Shares at the Placing Price to raise a total of £750,000 before expenses. Two of the Directors, John Savin and David Fell, have subscribed respectively for 50,000 and 300,000 Ordinary Shares under the Placing.

Further details of the Placing Agreement are set out in paragraph 5 of Part V of this document. The Placing Shares will rank *pari passu* with the existing Ordinary Shares including the rights to all dividends and other distributions declared paid or made after the date of issue.

The Company has also entered into a Put and Call Option Agreement with Billam AG and Billam plc ("the Optionholders") under which the Company can require the Optionholders to subscribe for up to 12,500,000 Ordinary Shares at the Placing Price. The Optionholders are entitled to receive a fee of £12,500 plus VAT payable in shares at the Placing Price. Further details of the Put and Call Option Agreement are set out in paragraph 5 of Part V of this document.

# 5. Lock-in Arrangements

Each of the Directors and EiRx Pharma has agreed with HB-corporate and the Company that they will not (except in the limited circumstances permitted by the AIM Rules including in the event of an intervening court order, the death of a Director, or in respect of the acceptance of a take-over offer of the Company which is open to all Shareholders) dispose of any Ordinary Shares in which they or any connected person are interested until the date which falls 12 months after the date of Admission.

# 6. Directors

The Directors of the Company are as follows:

*Dr Stephen Parker MBA, Chairman, aged 46*, joined the Board in March 2004 to assist in developing the Company and its strategy. He was Finance Director at Oxford GlycoSciences plc following a career in corporate finance with Apax Partners, SBC Warburg Dillon Read and ING Barings. He has also worked for PA Consulting and Unilever. Dr Parker holds a DPhil in Biochemistry from Oxford University and an MBA from City University.

*Dr John Savin MBA, Chief Executive Officer, aged 47*, was an International Product Manager in global marketing with Pharmacia, Amersham International and ICI Diagnostics. In 1989, he joined an innovative consultancy (Centre for Exploitation of Science and Technology) where his clients included Glaxo, Zeneca, Roche, the UK Cabinet Office and the Medical Research Council. In 1994 he joined Greig Middleton & Co later becoming a Director and Head of Biotechnology. Dr Savin left Greig Middleton, having co-founded e-phen and then joined Physiomics as Executive Director in July 2001. Dr Savin holds a doctorate in organic chemistry from the University of Nottingham.

*David Collins ACA, Finance Director, aged 48*, joined the Board as part-time Finance Director in May 2004. He is also part-time Finance Director at Gieves and Hawkes. Mr Collins qualified as a Chartered Accountant with Peat Marwick Mitchell & Co (now KPMG), following which he joined CDS Housing Association. His career spans a wide range of retail and industrial business including positions with BASF, ICI and Thorn EMI. Since 2001 Mr Collins has been undertaking short term financial management and consulting to a variety of corporate and government clients.

*Professor David Fell, Non-executive Science Director, aged 56*, holds a chair in, and is Assistant Dean of, the School of Biological and Molecular Sciences at Oxford Brookes University and is recognised as an expert in systems biology. Professor Fell runs a research team at Oxford Brookes University where current projects include the analysis of the structure of metabolic networks, the computer simulation of signal transduction and elementary modes for the analysis of metabolism and metabolic engineering. He is the author or co-author of approximately 85 scientific publications and has written one of the standard textbooks, "Understanding the Control of Metabolism" in the area of metabolic control analysis. Dr Fell has been involved with the Company since 2001.

Dr Paul Harper, Non-executive Director, aged 58, has over thirty years experience of the life sciences industry covering both drug development and medical devices. Dr Harper has served as Chief Executive of Cambridge Antibody Technology Limited and Provensis Limited. He has also served as Corporate Development Director of Unipath, then the medical diagnostics business of Unilever and as Director of Research and Development for Johnson & Johnson Limited. Formerly head of Antimicrobial Chemotherapy for Glaxo, Dr Harper holds a doctorate in molecular virology and is the author of over 50 publications. Dr Harper joined the Board in August 2004.

*John Pool, Non-executive Director, aged 60*, is Scottish Enterprise's Biotechnology Business Adviser and has extensive commercial and scientific experience in the health care, pharmaceutical and biotechnology sectors. He founded Proteus Molecular Design Limited which in 1990 was floated as Proteus International plc (now Protherics plc). A director of the AIM quoted The Medical House plc, EiRx Therapeutics plc and Zyzygy plc, John Pool is also a member of the advisory panel of Simfonec, which acts to assist a number of London colleges with their commercialisation as well as being a director of Nestech Limited, the University Challenge Seed Fund of the Universities of Aberdeen, Dundee and St Andrews. John Pool is also a director of EIRx Pharma, the controlling shareholder of the Company.

# 7. Scientific Advisory Board

The Scientific Advisory Board ("SAB") is responsible for critically reviewing the Group's scientific strategy. Its role will be to inform the Group of any scientific or technological advances that are relevant to Physiomics or its competitors, and provide links to a network of business, industrial and academic contacts.

The SAB will convene as required and its membership will be reviewed periodically. It is proposed that the initial members of the SAB will be:

Professor Marta Cascante, of the University of Barcelona, is an expert on systems biology and the development of metabolic simulations. She has a long standing interest in the metabolism of cancer cells.

Professor Tom Cotter, currently Professor of Biochemistry at the University of Cork, is an expert in the field of apoptosis and member of a number of governmental and non governmental scientific advisory bodies.

Physiomics has further established a network of scientists for advice and consultation. This constant interaction plays a critical function in the advancement of the Company's scientific knowledge base.

# 8. Share Option Schemes

The Directors believe that the Group's success is highly dependent on the quality of its employees. To assist in recruitment, retention and motivation of high quality key employees, the Group must have an effective remuneration strategy. The Directors consider that an important part of its remuneration strategy will be the ability to award equity incentives and, in particular, share options to key employees. Consequently the Directors intend to establish share option schemes for the benefit of the management and staff of the Group following Admission. The Directors intend that the schemes will be compliant with guidelines issued by institutional investment protection committees as appropriate to a group of its size.

# 9. Dividend policy

The Board believes that it is inappropriate to make a forecast of the likely level of any future dividends. However, the Board intends to commence the payment of dividends when it becomes commercially prudent to do so and to pursue a progressive dividend policy in line with earnings growth, subject to the availability of distributable profits, whilst retaining sufficient income for the Group's projected working capital requirements.

# **10.** Corporate Governance

The Board is committed to maintaining high standards of corporate governance. The Company intends to develop appropriate measures to ensure that it will be able to comply with the Combined Code so far as is practicable for a company of its size and stage of development. The Company also proposes to follow the Guidance for Smaller Quoted Companies on the Combined Code issued by the Quoted Companies Alliance in August 2004.

The Board has established a Remuneration Committee comprising the Chairman of the Company, and two non-executive Directors. The Remuneration Committee is chaired by Stephen Parker. The Remuneration Committee will review the performance of the executive Directors and determine the remuneration of the executive Directors and the basis of their service agreements with due regard to the interests of Shareholders. The Remuneration Committee will also determine the payment of any bonuses to executive Directors and the grant of options to employees, including executive Directors, in relation to any share option scheme adopted by the Company.

The Board has also established an Audit Committee comprising the Chairman of the Company, the Finance Director and one non-executive Director. The Audit Committee is chaired by Paul Harper. The Audit Committee will be responsible for ensuring that the financial performance, position and prospects of the Company are properly monitored, controlled and reported on and for meeting the auditors and reviewing their reports relating to accounts and internal controls.

The Directors have also considered the guidance published by the Institute of Chartered Accountants in England and Wales (commonly known as the Turnbull report) concerning the internal control requirements of the Combined Code. The Board will regularly review and manage key business risks in addition to financial risks facing the Company in the operation of its business.

The Company has adopted and will operate a share dealing code for Directors and senior employees on the same terms as the Model Code appended to the Listing Rules of the UKLA.

# 11. Majority Shareholder

Following Admission, the majority shareholder of the Company will be EiRx Pharma which will own 75.7 per cent. of the issued ordinary share capital of the Company. The Company and EiRx Pharma have, as

a matter of best practice, entered into a relationship agreement ("Relationship Agreement") as would be required under the Listing Rules of the UKLA if the Company were listed on the Official List. The Relationship Agreement is designed to ensure that the Company is capable at all times of carrying on its business independently of any controlling shareholder, managing its cash and assets independently and that all transactions and relationships in the future between the Company and any such controlling shareholder must be at arm's length and on a normal commercial basis.

Full details of the Relationship Agreement, including the circumstances in which the above undertakings cease to apply, are set out in paragraph 5 of Part V of this document.

The Directors are of the opinion that the Company will be at all times capable of carrying on its business independently of EiRx Pharma and that all transactions and relationships between the Company and EiRx Pharma are, and will be, at arm's length and on a normal commercial basis. Whilst there are currently no transactions contemplated between EiRx Pharma and the Company, in the event that any such transaction was proposed, EiRx Pharma has undertaken to ensure that such a transaction would be at arm's length and on a normal commercial basis and further that any EiRx Pharma directors who are also Directors of the Company would absent themselves from attending and voting at the Company's Board meetings on such matters. John Pool is currently a director of both the Company and EiRx Pharma.

Following Admission, it is not anticipated that EiRx Pharma will provide any services to Physiomics.

# Intentions with respect to shareholding

EiRx Pharma is subject to a lock-in agreement that is described above and in the Placing Agreement described in paragraph 5 of Part V of this document. It is EiRx Pharma's current intention to distribute its shareholding in the Company to its own shareholders following the end of its lock-in period.

# 12. Taxation

General information regarding UK taxation in relation to the Placing and Admission is set out in paragraph 8 of Part V of this document. If you are in any doubt as to your tax position you should consult your own financial adviser immediately.

# 13. CREST

The Company's Articles of Association permit it to issue shares in uncertificated form in accordance with the Uncertificated Securities Regulations 2001. CREST is a computerised share transfer and settlement system. The system allows shares and other securities to be held in electronic form rather than paper form, although a Shareholder can continue dealing based on share certificates and stock transfer forms. For private investors who do not trade frequently, this latter course is likely to be more cost effective.

The Directors will apply for the Ordinary Shares to be admitted to CREST with effect from Admission. Accordingly, settlement of transactions in Ordinary Shares following Admission may take place within the CREST system if the relevant Shareholders so wish. CREST is a voluntary system and holders of Ordinary Shares who wish to receive and retain share certificates will be able to do so.

# PART II

# INFORMATION ABOUT PHYSIOMICS' PRODUCTS, INTEGRATED SERVICES AND MARKETS

#### Introduction

Physiomics plc, in collaboration with BTS, uses the science of systems biology to sell products and services for optimisation of the drug development process with a particular focus on cancer therapies. The main benefits to customers, the Directors believe, are reduced rates of failure in clinical development and the associated cost savings.

Physiomics is also applying its technologies to two proprietary cancer development projects.

#### Co-operation agreement with Bayer Technology Services GmbH

Key to the Company's product offering is an agreement with Bayer Technology Services GmbH ("BTS") which integrates the two companies' complementary products The agreement has lead to further product development and joint global marketing. This agreement defines payment terms to Physiomics for non-exclusive access to Physiomics' novel patented technology platform and intellectual property. The agreement further provides for cross licensing and distribution of products and services including the non-exclusive right of Physiomics to use and market the BTS product PK-Sim<sup>®</sup>.

#### Marketing the integrated technologies

It is the belief of the Directors that systems biology can enable the correct pharmaceutical dose at the disease site to be predicted early in development. PK-Sim<sup>®</sup> software can then be used to evaluate how much drug is needed to achieve therapeutic levels at the target site.

To meet the perceived market demand for these services, Physiomics, in collaboration with BTS, is offering a range of services and partnering opportunities. Physiomics and BTS have conducted joint sales training so that a unified and common approach to sales is presented to the end user. Projects are all highly customised and work will be divided between the collaboration partners as appropriate with Physiomics normally leading biological modelling and BTS the drug delivery aspects.

Test marketing of this service has revealed a high level of interest for:

- the provision of services to optimise or troubleshoot clinical trials, typically requiring the use of both PK-Sim<sup>®</sup> and the sophisticated modelling supplied by Physiomics; and
- partnering and collaboration, where Physiomics is seeking partners to join a technology collaboration on a next generation cancer therapy development environment.

#### The Drug Discovery and Development Process

New drugs are frequently developed to compete in established markets where in order to succeed they must offer distinct advantages over existing products. These advantages normally provide for greater efficacy, less frequent dosing, lower dose levels (hence reduced side-effects), and more efficient methods of delivery to the disease site. The discovery process needed to evaluate these properties (pharmacodynamic and pharmacokinetic) of the selected compounds traditionally makes use of *in vitro* and classical *in vivo* (animal) models in order to identify the most appropriate drug candidate(s). Whilst these *in vivo* model systems may crudely mimic the disease process in man, the scale and physiology of the test animals is different from man and unless considerable investment is made to validate the model, it is usually only possible to rank compounds in terms of particular properties, such as half life or peak drug level, There is no guarantee that this ranking will in any way reflect the performance of the drug in the human patient.

Once a candidate compound has been selected, the molecule enters pre-clinical toxicology. This process is designed to evaluate the toxicity of the drug in animals and to provide guidance as to the most appropriate route of administration, dosage level and dosage frequency. Pilot studies are required to allow protocols for the main studies to be designed. These add cost, time and consume supplies of expensive prototype drugs.

The Physiomics technology can be used in the earlier stages of drug discovery to compare the pharmacological profile of potential drug candidates and indicate the optimal dosage regimen and route of delivery. This provides comparative data and permits the early progression of molecules that best fit the USP for a successful product. Physiomics technology can also be used to supplement *in vivo* or *in vitro* tests.

The technologies are also applicable (and potentially more valuable) once a compound enters pre clinical testing and also the Phase I and II stages of clinical development. The simulations can be calibrated to identify the optimal clinical development route. SystemCell<sup>TM</sup> and systems biology technology can be used to determine how much active drug needs to be maintained at the disease site. PK-Sim<sup>®</sup> can be used to determine the dosing regimen that delivers optimum therapeutic drug levels at the disease site. These two technologies, pharmacodynamic and pharmacokinetic simulations, are described below. They are being further developed as an integrated suite of services and products. The data generated is used to define the parameters of pre-clinical and clinical research protocols with the aim of producing "right first time" studies in those fields of drug development that are expensive and time consuming to repeat.

#### Pharmacodynamics

Finding the dose at which a therapeutic agent has optimal effect while minimising its toxic effects is the key challenge of any clinical trial. At the outset of a clinical development process, there is often little direct data to indicate the correct dose of a new therapy. Animal studies provide early indications. These studies are legally necessary but the results are an unreliable guide to human trials. The Directors anticipate that the use of *in silico* techniques will enable Physiomics' customers to reduce the number of animal experiments per lead compound under development.

Physiomics constructs mathematical simulations of biological processes using ordinary differential equations (ODE). These simulations are designed to emulate the best and latest understanding of the biology. The scientific basis of this approach is systems biology, the understanding of how proteins and genes, as components of an overall pathway and network, interact to generate biological function.

Physiomics has, as its core simulation, a mathematical description of the mammalian cell cycle designed for pharmaceutical applications. This simulation was the subject of a DTI SMART award in 2002. The simulation was created together with Cyclacel, a Scottish cancer drug development company. The Directors are only aware of one other company claiming to possess a pharmaceutically relevant cell cycle simulation.

Other simulations under development include the MAP Kinase cascade, a standard signalling route used by many cancer cells to respond to growth signals, PI3 Kinase signalling (a method used by cancer cells to avoid death and enhance growth) and a model of the biochemistry of programmed cell death (apoptosis).

Current research will see the Company further developing and linking these simulation models into a holistic representation of a population of cancer cells that can be tailored to individual patients, and to which existing cancer drugs and new therapeutic approaches, such as GeneICE can be applied.

Whilst the current therapeutic focus is in cancer, the Company intends to further expand its set of simulations as a core platform. Other areas could include autoimmune diseases such as rheumatoid arthritis, type II diabetes and strategies for anti-viral therapies.

#### Pharmacodynamic Software

Physiomics is presently conducting single cell simulations for clients. However, it is developing a multi-cellular model based on a patented technology, SystemCell<sup>TM</sup>, to create virtual biological cell populations, where each cell encapsulates its own copy of the simulation. SystemCell<sup>TM</sup> software allows a virtual cell to be created and grown in a computer model. Each virtual cell contains a data set representing cell cycle proteins and genes and a set of mathematical equations representing their associated reactions. As the cell cycle completes, the software object representing the cell "divides" to create a new object or "cell" based on its parent. Each of these objects is autonomous and random mutation events can be programmed into both objects to enable a diverse population of cells to develop. Many thousands of virtual cells can be grown in a standard desktop computer allowing the creation of virtual tumour masses.

The advantage of using a population of virtual cells rather than one individual model cell is that cancer treatment only acts on cells in a vulnerable state of the cell cycle. Thus the software mimics the situation observed in real tumours which require multiple courses of chemotherapy to kill the cancer cells.

When pharmacokinetic drug profiles are applied to a virtual tumour, the effects of different doses, therapeutic combinations and timing can be seen. By combining SystemCell<sup>TM</sup> and PK-Sim<sup>®</sup>, the integrated system can also be customised to take into account variations in patient weight, body characteristics, the genetic type of their normal and cancer cells and is designed to enable a new therapy to be tested and optimised in combination with existing therapies — as happens in actual clinical practise.

The Directors believe that as this technology is further developed and tested in clinical situations, it will become possible to predict clinical trial outcomes. This may help refine the trial design to improve the probability of a successful outcome and a shorter route to approval and launch.

# Pharmacokinetics

PK-Sim<sup>®</sup> uses a range of physico-chemical experimental measurements on drug molecules to produce accurate pharmacokinetic data within a sophisticated software environment. PK-Sim<sup>®</sup> enables overall drug behaviour within the patient to be understood: the absorption, metabolism, distribution and excretion (ADME).

Current pharmacokinetic studies of a pharmaceutical take data from animal models and extrapolate this to man. This is a crude and approximate process. As a result several experiments in volunteers (Phase I) are required to refine the ADME data and provide the basis for design of therapeutic (Phase II) studies. This is an expensive but essential step. The Directors believe that the number and extent of such Phase I studies can be significantly reduced by using PK-Sim<sup>®</sup> to predict the optimal dose regimen in man. Calibrating and adjusting models is a high-value service offering. Once calibrated, PK-Sim<sup>®</sup> allows different chemical properties and formulations to be evaluated and dosing schedules to be optimised.

Leading pharmaceutical companies are potential or actual PK-Sim<sup>®</sup> customers and are increasingly recognising the value of the new physiology-based modelling approaches. Smaller companies including mid-sized pharmaceutical and biotechnology companies, which are also potential customers, are more likely to buy in services and consultancy as required, rather than buy a license outright and this is the market Physiomics intends to focus on.

# **Proposed services**

# Introduction

A clinical trial is designed around a planned statistical analysis that is based on best estimates of the likely outcome of treatment. The endpoints are defined and patient numbers selected to meet the clinical objective.

Once the trial is analysed statistically, the study will only be considered successful if the primary endpoint is met within the statistical confidence boundaries. Regulatory agencies usually require, in addition to Phase I and Phase II studies, two pivotal Phase III Studies. Physiomics provides services to:-

- Optimise trial design and maximise the chances of a successful outcome;
- Troubleshoot problem trials, identify the remedial action required and salvage drug development programmes; and
- Evaluate in-licensing opportunities where a better understanding of the drug and improved risk/benefit assessment analyses will help shape the deal.

# Optimising trial design

The target markets for this application are Phase I and II studies where dose and dose responses are assessed. Drug companies need to establish the effective level of the dose at the disease site and the dosing frequency required to sustain an effective drug concentration.

The Directors believe that there are currently more than 800 active Phase I projects in progress typically completing within a 12 month period. They also believe there are also more than 1,000 Phase II projects running, each lasting in the region of 2 years. Approximately 65 to 70 per cent. of Phase II trials will fail, as a result of researchers' inability to find a safe dose of drug that shows an effective clinical response.

The use of systems biology approaches should enable a better understanding of the pharmacodynamics of efficacy, dose and elimination profiles for new drugs well before clinical testing.

#### Troubleshooting problem trials

It has been shown that 30 per cent. of tested drugs fail as they do not exhibit a clinical response, 39 per cent. fail due to delivery problems and a further 11 per cent. fail due to a combination of poor toxicology, delivery and efficacy.

The use of the combined Physiomics-BTS technologies enables the assessment of individual patients and their drug responses to be examined in detail from the data produced in the clinical trial. Alternative trial designs could then be suggested and evaluated in focused Phase II studies. Physiomics is in discussion about one such project.

# Evaluating in-licensing opportunities

Physiomics is able to provide services to those pharmaceutical companies wishing to further evaluate their candidates prior to selection and/or to those seeking to "buy in" (in licence) potential therapeutics but who intend to further evaluate their potential. Conversely, biotechnology and small pharmaceutical companies looking to partner their candidates with major pharmaceutical companies might wish to undertake an in depth evaluation of their portfolio prior to out-licensing a candidate in order to maximise potential values.

### In-house drug development

The market for cancer related therapies is worth approximately \$14 billion per year. The market is continually evolving with 10 million additional patients being diagnosed annually worldwide of whom 1.3 million are in the USA.

Physiomics has started to develop proprietary cancer therapeutics using its combined core technologies. The selected area uses a novel gene silencing technology known as GeneICE developed at Imperial College London. Physiomics has obtained a 2 year option for a licence from Cronos Therapeutics Limited.

# GeneICE technology

The GeneICE technology is delivered through the use of liposomes, small synthetic fat vesicles that are taken up by cells. These can be further engineered to target cancer cells. Once taken up, the GeneICE construct is designed to enter the cell nucleus to bind to one or more genes very specifically. Once this happens, the bound genes can be silenced by the action of an enzyme naturally present in the cells, histone deactylase. In contrast, technologies like antisense and siRNA must act on the RNA products of the gene. There are many more copies of these molecules whereas a normal cell only has two copies of any gene. As a consequence, antisense and siRNA need to deliver potentially larger doses of therapeutic continuously to have an effect.

# Using GeneICE in cancer

The GeneICE approach contrasts favourably with the small molecule approach in that it has built-in specificity. This could minimise the toxicity problems frequently observed in the development of many cancer therapeutics. However, to be effective, the right GeneICE targets need to be selected. Physiomics is using its simulation of the cell cycle to select targets that will have a major impact on the cancer cell's ability to divide and will help to trigger cell death (apoptosis). Specific GeneICE molecules will then be made and tested in a quantitative cell biology experimental system to check the correspondence between simulation and experimental results. This approach will be combined with existing cancer therapies as required.

Specific GeneICE constructs undertaken for Physiomics may have unique DNA sequences and are therefore potentially patentable by Physiomics.

# Competition

Physiomics now competes in two markets:

- pharmacokinetic products and services; and
- systems biology and pharmacodynamic services.

# Pharmacokinetic competitors

Pharsight Inc. sells software and services to optimise the design of clinical trials using statistical methods. It also sells a product to carry out classic mathematical analysis of PK data. Pharsight posted sales of \$17.7 million during their financial year ended 2004, \$9.6 million from services and \$8.1 million from software sales and lease renewals. Pharsight is growing at approximately 30 per cent. per annum.

#### Systems biology competitors

There are a number of companies that create and analyse large biological data sets, such as Beyond Genomics, or Cellzome a drug discovery company building a research and development pipeline in chronic diseases. Neither, however, offer simulations.

Some simulation companies target bacterial systems and optimise fermentation processes for food, pharmaceutical and speciality chemical production, for example, INSILICO biotechnology GmbH (Germany) and Genomatica (US). Some companies like InNetics AB are believed to have developed commercial software to construct biochemical pathway models.

Entelos Inc, based in California, is believed to be the current market leader. A very sophisticated decision analysis package is tailored to different disease states to create Physiolabs. The principle product lines focus on diabetes, obesity and inflammatory diseases such as asthma. The approach is useful in target validation.

Gene Network Sciences Inc (GNS) is located on the US East Coast. The company has a strong cancer focus using a visualisation tool (Visual Cell) to diagram pathways and visualise complexity. Gene Network identifies its market as increasing the chances of success in Phase II and III trials. The company integrates biological and chemical data to create computer models of cell function and human biology. GNS believes that systems biology will double the "chance of success" in pharmaceutical development. The company intends to develop scaleable single cell models.

#### PART III

#### **RISK FACTORS**

In addition to the other relevant information set out in this document, the following specific factors should be considered carefully in evaluating whether to make an investment in the Company. The investment offered in this document may not be suitable for all of its recipients. If you are in any doubt about the action you should take, you should consult a person authorised under the Financial Services and Markets Act 2000 who specialises in advising on the acquisition of shares and other securities.

It should be noted that the risks described below are not the only risks faced by the Company. There may be additional risks that the Directors currently consider not to be material or of which they are currently unaware.

#### Stage of the Company's development

The Company is at an early stage of development and its business strategy is not proven. In particular, it has a very limited track record of sales. The Company may not be able to generate a sufficient number of contracts to satisfy its objectives. Further, even if the Company is able to generate a sufficient number of contracts, the value and profitability of those contracts may not be sufficient to ensure the long term viability of the business.

In common with many early stage businesses, the Company is dependent on the active involvement of the Board in all aspects of the Company's affairs. As the Company grows, it may face difficulties in establishing a suitable management structure for a larger company and in recruiting suitably skilled and qualified staff.

#### **Reliance on agreement with BTS**

The Company has entered into an agreement with BTS which creates a relationship which is of central importance to the current strategy and of importance to the research and development capabilities of the Company. The technology development and marketing aspects of the agreement cannot be terminated before 20 March 2006 except in certain limited circumstances. However, termination could have a significant effect on the future growth and profitability of the Company. Furthermore, there is no guarantee that such a collaboration will be successful. However, Physiomics could mitigate this risk by entering into other collaborations and by developing other marketing channels.

The agreement with BTS is non exclusive. BTS could enter into similar agreements with other suppliers of PD systems. This could reduce the support that BTS gives to the their alliance, impacting adversely on sales and reducing profits or increasing losses.

#### **Intellectual Property Risk**

The Group faces the risk of not being able to protect its own intellectual property, or of being forced to initiate litigation to protect its position which may take time and money to resolve.

The Group owns a patent in respect of SystemCell<sup>TM</sup> in the United States and the corresponding European patent has been assigned to Physiomics in a number of European countries. However, registration of the assignment has not yet been recorded at the various European national patent offices. While the Group is able to use technology covered by the patent, it cannot prevent other parties from using the technology in Europe until the assignments have been so recorded. While the Company is seeking to effect registration of the assignment, there is no guarantee that this will happen in any or all of the European countries in question.

While the Directors do not believe that there are any patents that cover its area of activity and which would prevent it operating within that area, the Group may also find itself the subject of litigation by other parties who believe that the group is infringing patents of which the Group is not yet aware.

#### Competition

While the Directors believe that Physiomics has a set of skills that may be unique, the Company may face competition from companies in business at present or not yet established that are better funded, staffed or equipped than the Company. There is also a risk that the Company's target customers, pharmaceutical companies, may choose to set up similar operations. Competition from any source would adversely affect the Company's ability to generate income.

# Technology

The Company may come to face competition from other businesses that possess skills and technologies that are not known or available at present. Such competition could prevent the Company from achieving sales. Differential equations are not the only way to model biological systems. Other mathematical/computing techniques include graph theory, control theory and cellular automata. It is therefore possible that there exists a competitor company not known to the Directors because its technologies are a long way from the Company's expertise.

# Accuracy

The technology has not been used in conjunction with actual clinical trials to compare results allowing assessment of the accuracy of the technology. Validation of the Physiomics' technologies will require work done in parallel with an actual clinical trial, something that is part of Physiomics' development plan. Until that is the case the accuracy of the results may be questioned and will still require the expenditure of clinical trials to support, or possible conflict with, the results.

# Dependence on key personnel

The Company's future success is substantially dependent on its senior management, the loss of any of whom could affect the Company's development. To mitigate this risk, the Company intends to introduce a share option scheme following Admission. Nonetheless, the Company faces a risk of losing key employees.

# Legal and contractual risks

All agreements are subject to interpretation and some agreements are not binding. There is no guarantee that the Company will be able to enforce all its rights under its agreements or arrangements with third parties.

# Subsequent fundraising

The Company may need to raise additional future funding in order to carry out its business strategy and possibly to continue trading. There is no guarantee that such funds will be forthcoming.

# **Regulatory and legal changes**

The Company strategy has been formulated in the light of the current regulatory and legal environment and likely future changes. The regulatory and legal environment may change in the future and such changes may have a material adverse effect on the business.

Existing and possible future environmental legislation, regulations and actions could cause additional expense, capital expenditures, restrictions and delays in the activities of the Company, the extent of which cannot be predicted.

#### General economic conditions

Changes in the general economic climate in which the Company operates may adversely affect the financial performance of the Company. Factors which may contribute to that general economic climate include the level of direct and indirect competition against the Company, industrial disruption, interest rates and the rate of inflation.

# Exchange Rate Risk

The Directors anticipate that a number of potential future contracts will be denominated in US Dollars or Euros. If either of those currencies was to fall relative to Sterling, the profitability of those contracts could be adversely affected.

# Liquidity of the Ordinary Shares

Admission to AIM should not be taken as implying that there will be a liquid market for the Ordinary Shares. It may be more difficult for an investor to realise his or her investment on AIM than to realise an investment in a company whose shares are quoted on the Official List. An investment in the Ordinary Shares may therefore, in certain circumstances, be difficult to realise.

The price at which investors may realise their holding of Ordinary Shares and the timing of any disposal of them may be influenced by various factors, some of which are specific to the Company and others of which are extraneous. Investors may not get back the whole of their investment.

# PART IV

#### FINANCIAL INFORMATION

### ACCOUNTANTS' REPORT ON PHYSIOMICS PLC

# Grant Thornton 🕏

The Directors Physiomics plc The Magdalen Centre Oxford Science Park Robert Robinson Avenue OXFORD OX4 4GA

and

Grant Thornton Corporate Finance Grant Thornton House Melton Street Euston Square LONDON NW1 2EP

and

The Directors HB-corporate 40 Marsh Wall LONDON E14 9TP

15 December 2004

#### PHYSIOMICS PLC ("THE COMPANY")

#### 1. Introduction

1.1 We report on the financial information set out in paragraphs 3 to 7. This financial information has been prepared for inclusion in the AIM admission document dated 15 December 2004.

#### Basis of preparation

- 1.2 The financial information set out in paragraphs 3 to 7 below is based on the audited statutory financial statements of the Company for the two periods ended 31 December 2001 and 30 June 2003 and for the year ended 30 June 2004 and has been prepared on the basis set out in paragraph 3 after making such adjustments as we considered necessary.
- 1.3 For the purposes of paragraphs 3 to 7 below the following abbreviations have been made:
  - 2001 7 months ended 31 December 2001
  - 2003 18 months ended 30 June 2003
  - 2004 year ended 30 June 2004

#### Responsibility

- 1.4 Such financial statements are the responsibility of the directors of the Company who approved their issue.
- 1.5 The directors of the Company are responsible for the contents of the AIM admission document dated 15 December 2004 in which this report is included.
- 1.6 It is our responsibility to compile the financial information set out in our report from the financial statements, to form an opinion on the financial information and to report our opinion to you.

Grant Thornton UK LLP is a limited liability partnership registered in England and Wales: No.OC307742. Registered office: Grant Thornton House, Melton Street, Euston Square, London NW1 2EP. A list of members is available from our registered office.

Grant Thornton UK LLP is authorised and regulated by the Financial Services Authority for investment business.

#### Basis of opinion

- 1.7 We conducted our work in accordance with the Statements of Investment Circular Reporting Standards issued by the Auditing Practices Board. Our work included an assessment of evidence relevant to the amounts and disclosures in the financial information. The evidence included that previously obtained by the auditors relating to the audit of the financial statements. Our work also included an assessment of significant estimates and judgements made by those responsible for the preparation of the financial statements underlying the financial information and whether the accounting policies are appropriate to the entity's circumstances, consistently applied and adequately disclosed.
- 1.8 We planned and performed our work so as to obtain all the information and explanations which we considered necessary in order to provide us with sufficient evidence to give reasonable assurance that the financial information is free from material misstatement whether caused by fraud or other irregularity or error.

#### Opinion

1.9 In our opinion the financial information gives, for the purposes of the AIM admission document dated 15 December 2004, a true and fair view of the results and cash flows of the Company for the two periods ended 31 December 2001 and 30 June 2003 and for the year ended 30 June 2004 and of the state of affairs of the Company at the end of each of those periods.

#### Consent

1.10 We consent to the inclusion in the prospectus dated 15 December 2004 of this report and accept responsibility for this report for the purposes of paragraph 45(1)(b)(iii) of Schedule 1 to the Public Offers of Securities Regulations 1995.

#### 2. Statutory Information

2.1 The Company was incorporated on 30 May 2001.

#### 3. Accounting policies

#### Basis of accounting

The financial information was prepared under the historical cost convention and in accordance with applicable United Kingdom accounting standards.

#### Consolidation

In the opinion of the Directors, the results of the subsidiary e-phen Limited, which has been dormant since May 2003, are immaterial (see note 7g) and consequently group accounts have not been prepared. This financial information therefore reflects the trading of Physiomics plc only.

#### Going concern

In the preparation of the financial information for the year ended 30 June 2004 on a going concern basis, cashflow forecasts and working capital requirements for the 12 month period from the date of Board approval of the financial statements were prepared by the Directors. As detailed in note (x), the Company entered into a placing agreement conditional, *inter alia*, on admission, for ordinary shares on 15 December 2004.

For those reasons, the directors believe that it is appropriate to prepare the financial statements on a going concern basis, which assumes that the Company will continue in operational existence for the foreseeable future.

#### Turnover

Turnover is the total amount receivable by the Company for goods and services provided, excluding VAT and trade discounts.

#### Investments

Investments are included at cost less amounts written off.

# Research and development

Research and development expenditure is written off in the year in which it is incurred. Development costs incurred on specific projects are capitalised when recoverability can be assessed with reasonable certainty and amortised in line with the expected sales use arising from the projects. All other development costs are written off in the year of expenditure.

# Operating lease agreements

Rentals applicable to operating leases where substantially all of the benefits and risks of ownership remain with the lessor are charged against profits on a straight line basis over the period of the lease.

# Grants

Grants received in respect of revenue expenditure are matched against related costs in the year in which these costs occur.

# Fixed assets

Tangible fixed assets comprising fixtures, fittings and IT equipment are depreciated over 3 years.

# Intangible fixed assets

Patents and trademarks purchased are included at cost and amortised over their useful economic lives which is estimated to be 15 years.

# 4. Profit and loss accounts

		2001	2003	2004
	Note	£'000	£'000	£'000
Turnover			50	62
Other operating income			38	7
Administrative expenses	_	(137)	(355)	(299)
Operating loss		(137)	(267)	(230)
Amounts written off investments	_	(5)		
Loss on ordinary activities before taxation		(142)	(267)	(230)
Tax on loss on ordinary activities	7(b)		8	5
Loss for the financial period	_	(142)	(259)	(225)
Basic loss per share	7(d)	(8.0p)	(4.7p)	(3.4p)

The Company has no recognised gains or losses other than the losses stated above.

All of the Company's activities continued during the periods.

The accompanying notes form an integral part of this financial information.

# 5. Balance sheets

		2001	2003	2004
	Note	£'000	£'000	£'000
Fixed assets				
Intangible assets	7(e)	65	63	58
Tangible assets	7(f)	1	4	13
Investments	7(g)			
		66	67	71
Current assets				
Debtors	7(h)	25	9	13
Cash at bank and in hand		48	3	9
		73	12	22
Creditors: amounts falling due within one year	7(i)	(9)	(39)	(447)
Net current assets/(liabilities)		64	(27)	(425)
Creditors: amounts falling due after more than one year	7(j)		(169)	
Net assets/(liabilities)		130	(129)	(354)
Capital and reserves				
Called up share capital	7(k)	22	67	67
Share premium account	7(1)	250	205	205
Profit and loss account	7(1)	(142)	(401)	(626)
Shareholders surplus/(deficiency)	7(m)	130	(129)	(354)

The accompanying notes form an integral part of this financial information.

# 6. Cash flow statements

	Note	2001 £'000	2003 £'000	2004 £'000
Net cash outflow from operating activities	7(n)	(153)	(211)	(218)
Taxation Capital expenditure and financial investment			8	
Purchase of tangible fixed assets		(1)	(6)	(12)
Purchase of intangible fixed assets		(65)	(5)	_
		(66)	(11)	(12)
Management of liquid resources Purchase of investments		(5)	_	_
Financing Issue of ordinary shares		272	_	_
Net cash inflow from related parties			169	236
		272	169	236
Increase/(decrease) in cash	7(o)	48	(45)	6

The accompanying notes form an integral part of this financial information.

# 7. Notes to the financial information

(a) Loss on ordinary activities before taxation

The loss on ordinary activities before taxation is stated after:

	2001 £'000	2003 £'000	2004 £'000
Research and development:			
Current year expenditure	53	58	53
Auditor's remuneration:			
Audit services	2	2	2
Depreciation and amortisation:			
Tangible fixed assets, owned		3	
Intangible fixed asset		7	

# (b) Directors and employees

Staff costs during the periods including Directors' fees were as follows:

	2001 £'000	2003 £'000	2004 £'000
Wages and salaries	32	145	84
Social security costs	3	15	9
	35	160	93

The average number of employees including Directors during the periods was 5 (2003: 3, 2001: 2).

Remuneration in respect of Directors was as follows:

	2001	2003	2004
	£'000	£'000	£'000
Aggregate emoluments	32	110	57
	32	110	57

No Directors participated in any pension scheme.

The emoluments paid to the individual Directors were as follows:

	2001	2003	2004
	£'000	£'000	£'000
Dr John Savin	22	75	50
Professor David Fell	10	35	
Dr Stephen Parker		_	6
David Collins			1
	32	110	57
(c) Taxation			
	2001	2003	2004
	£'000	£'000	£'000
Current tax			
R & D tax credit in respect of prior year		(8)	(5)
	—	(8)	(5)

Unrelieved tax losses of £280,000 (2003: £77,000) (2001: £Nil) remain available to offset against future trading profits.

# (1) Factors affecting the tax charge

The tax assessed for the period is higher than the standard rate of corporation tax that would result from applying the standard rate of United Kingdom corporation tax to the loss on ordinary activities. The differences are explained as follows:

	2001	2003	2004
	£'000	£'000	£'000
Loss on ordinary activities before tax	(142)	(267)	(230)
Loss on ordinary activities multiplied by standard rate of			
corporation tax of 19% (2003: 19%)	(27)	(51)	(44)
Effects of:			
Expenses not deductible for tax purposes	6	5	1
Utilisation of tax losses	21	46	43
R & D tax credit in respect of prior year		(8)	(5)
Current tax charge		(8)	(5)

# (d) Loss per ordinary share

The calculation of earnings per ordinary share is based on the following:

		Weighted average		
	Loss for the year	number of shares	Loss per share	
2001	£(142,000)	1,781,750	(8.0p)	
2003	£(259,000)	5,470,696	(4.7p)	
2004	£(225,000)	6,714,036	(3.4p)	

There is no dilutive effect on the loss per share and consequently this has not been calculated.

#### (e) Intangible fixed assets

	2001 £'000	2003 £'000	2004 £'000
<b>Cost</b> At start of period Additions	65	65 5	70
At end of period	65	70	70
Amortisation At start of period Charge		7	7 5
At end of period		7	12
Net book value at end of period	65	63	58

Intangible fixed asset cost includes the cost of obtaining and exercising an option over the SystemCell<sup>TM</sup> software and patent.

# (f) Tangible fixed assets

	2001	2003	2004
	£'000	£'000	£'000
Cost			
At start of period		1	7
Additions	1	6	12
At end of period	1	7	19
Amortisation			
At start of period			3
Charge		3	3
At end of period		3	6
Net book value at end of period	1	4	13

Tangible fixed assets include fixtures, fittings and computer equipment.

# (g) Investments

# Fixed asset investments

in group	
ertaking	Total
£'000	£'000
5	5
5	5
	2rtaking £'000 5 5 

At 30 June 2004 the Company held 20 per cent. or more of the allotted share capital of the following:

	Class of share	Proportion	Nature of
	capital held	held	business
e-phen Limited	Ordinary	100%	Consultancy

The aggregate amount of capital and reserves of e-phen Limited at 31 March 2001 was £969. The profit for the year ended 31 March 2001 was £169. The aggregate amount of capital and reserves of e-phen Limited at 31 May 2002 was £2,817 including a share issue of £3,600. The unaudited loss for the period from 1 April 2001 to 31 May 2002 was £1,752. The unaudited loss for the period from 1 June 2002 to 31 May 2003 was £868 and the capital and reserves at 31 May 2003 were £1,949. The company was dormant from May 2003.

### (h) Debtors

2001	2003	2004
£'000	£'000	£'000
24	6	1
		5
1	3	7
25	9	13
	$   \begin{array}{r}     2001 \\     \pounds'000 \\     24 \\     \\     1 \\     25   \end{array} $	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$

# (*i*) Creditors: amounts falling due within one year

	2001	2003	2004
	£'000	£'000	£'000
Trade creditors	1	35	28
Amounts owed to parent undertaking			314
Amounts owed to related parties			91
Social security and other taxes	3	3	5
Accruals	5	1	9
	9	39	447

Amounts due to parent undertaking and related parties at 30 June 2004 are interest free and repayable on demand. There are no formal conversion rights attached to the loans however these balances have been converted in full to ordinary shares in Physiomics plc as part of the Company's admission to trading on AIM.

Certain amounts due to related parties were converted into amounts due to the Company's parent, EiRx Pharma Limited, following a share issue in that company for which the balance due to these related parties formed part of the consideration for the issue of those shares.

See note 7(u) and note 7(x) for details of related party transactions and post balance sheet events.

# (*j*) Creditors: amounts falling due after more than one year

	2001	2003	2004
	£'000	£'000	£'000
Amounts owed to related parties		169	
		169	
(k) Share capital			
	2001	2003	2004
Authorized	£'000	£'000	£'000
1,000,000,000 Ordinary shares of £0.01 each	100	100	100
Allotted, called up and fully paid:			
6,714,036 (2001: 2,238,012) Ordinary shares of £0.01 each	22	67	67

In the period to 31 December 2001 the Company made the following allotments of share capital:

- on incorporation the Company made an allotment of 2 ordinary shares of £1 each;
- on 26 July 2001 the nominal value of the authorised and issued share capital was changed from £1 to 1 pence and authorised share capital was increased by £9,950,000;
- on 26 July 2001 1,319,800 ordinary 1 pence shares were issued at 4 pence each and 440,000 1 pence ordinary shares were issued at 4 pence each; and
- on 10 September 2001 33,570 ordinary shares of 1 pence each were issued as consideration for the intangible asset and valued at 45 pence each and 444,442 ordinary 1 pence shares were issued at 45 pence each.

The difference between the total consideration of  $\pounds 272,427$  and the nominal value of  $\pounds 22,380$  was credited to the share premium account.

On 7 March 2002, the Company capitalised £44,780 credited to the share premium account by the allotment of two ordinary shares of 1 pence each for every one ordinary share currently held by each member.

There were no allotments of shares during the year ended 30 June 2004.

# (1) Share premium account and reserves

						Share	Profit
					р	remium	and loss
						account	account
						£ 000	£ 000
At 29 May 2001						250	
Premium on issue of shares	to 21 Docom	or 2001				250	(142)
Retained loss for the period		2001					(142)
At 31 December 2001						250	(142)
Retained loss for the period	to 30 June 20	03					(259)
Premium used for allotment	during the pe	eriod				(45)	
At 30 June 2003						205	(401)
110 50 5 dile 2005						200	(101)
Retained loss for the year to	30 June 2004						(225)
At 30 June 2004						205	(626)
(m) Reconciliation of move	ements in sha	reholders	funds/(defic	ciency)			
				, 2	2001	2003	2004
				£	'000	£'000	£'000
Retained loss for the financia	al year/perio	d			(142)	(259)	(225)
Issue of shares					272		
Net increase/(decrease) in sh	nareholders' f	funds/(det	ficit)		130	(259)	(225)
Opening shareholders' funds	s/(deficit)		,			130	(129)
Closing shareholders' funds	(deficit)				130	(129)	(354)
	()					()	()
( <i>n</i> ) Net cash (outflow) fro	<i>m</i> operating	activities					
	1 0			, 2	2001	2003	2004
				£	'000	£'000	£'000
Operating loss					(137)	(267)	(230)
Depreciation and amortisati	on				_	10	8
Increase in creditors					9	30	3
(Increase)/decrease in debto	rs				(25)	16	1
Net cash outflow from operation	ting activitie	s			(153)	(211)	(218)
(o) Reconciliation of net c	ash flow to m	ovement i	n net funds/ (	(debt)			
				- 	2001	2003	2004
				£	'000	£'000	£'000
Increase/(decrease) in cash i	n the year				48	(45)	6
Cash inflow from other long	term creditor	rs				(169)	(236)
Movement in net funds in th	e year				48	(214)	(230)
Net funds/(debt) at beginnin	ng of period				_	48	(166)
Net funds/(debt) at end of p	eriod				48	(166)	(396)
(p) Analysis of changes in	net funds/(d	lebt)					
	At	,	At 31		At		At
	29 May	Cash-	December	Cash-	30 June	Cash-	30 June
	2001	flow	2001	flow	2003	flow	2004
	£'000	£'000	£'000	£'000	£'000	£'000	£'000
Cash in hand and at bank		48	48	(45)	3	6	9
Debt				(169)	(169)	(236)	(405)
	—	48	48	(214)	(166)	(230)	(396)

# (q) Capital commitments

There were no capital commitments at 30 June 2004, 30 June 2003 or 31 December 2001.

# (r) Contingent liabilities

There were no contingent liabilities at 30 June 2004, 30 June 2003 or 31 December 2001.

### (s) Leasing commitments

There were no finance leasing commitments at 30 June 2004, 30 June 2003 or 31 December 2001.

At 30 June 2004 the Company occupied premises on the Oxford Science Park and pay rent and charges at a current rate of £34,000 per annum. The commitment is for less than one year.

# (t) Controlling related party

The Directors consider EiRx Pharma Limited, a company incorporated in England and Wales, to be the ultimate parent company, by way of its majority share holding in Physiomics plc.

The only group undertaking for which group accounts have been drawn up is that headed by EiRx Pharma Limited. Copies of the group accounts can be obtained at 32 Clerkenwell Green, London EC1R 0DU

#### (u) Related Party Transactions

The Company was under the control of EiRx Pharma Limited throughout the current and previous year.

During the year ended 30 June 2004 the company incurred management charges and recharged expenses of  $\pm 145,056$  from Billam plc (2003  $\pm 34,329,2002 \pm Nil$ ).

During the year ended 30 June 2004 the company incurred management expenses from Peter Hoskins, a former director, of  $\pounds$ 53,575.

At 30 June 2004 Physiomics plc owed £84,535 to Peter Hoskins, a director of EiRx Pharma Limited and certain other entities under his control, in respect of loans and management charges to Physiomics plc.

At 30 June 2004 Physiomics plc owed £6,000 to Wellbeach Limited, a company incorporated in England and Wales that is under the control of John Pool, a director of EiRx Pharma Limited.

Since the year end consultancy and other fees of £167,865 have been charged by related parties for services in the period. These fees are being satisfied as part of the share issue on 6 December 2004.

# (v) Financial instruments

The Company finances its operations by raising finance through equity and borrowings. No speculative treasury transactions and no derivative contracts were entered into. Financial assets and liabilities include those assets and liabilities of a financial nature, namely cash and borrowings. Short term debtors and creditors have been excluded from the following disclosures.

#### Interest rate risk

The Company finances its operations principally from equity funding and loans. No interest was chargeable on the loans. There was no interest rate exposure during the periods.

#### Liquidity risk

The Company seeks to manage financial risk, to ensure sufficient liquidity is available to meet foreseeable needs and to invest cash assets safely and profitably.

The Company's policy throughout the periods has been to ensure continuity of funding by a combination of equity funding, grant income and loans.

# Maturity of financial liabilities

The Company's financial liabilities analysis was as follows:

	2001	2003	2004
	£'000	£'000	£'000
In less than one year or on demand			
Amounts due to parent undertaking			314
Amounts owed to related parties			91
In more than one year			
Other loans		169	
		169	405

#### Fair values

Fair values of financial instruments equate to the book value as disclosed in the financial information.

There are no material differences between the fair value of financial instruments and the amount at which they are stated in the accounts. This is due to the fact that they are of short maturity and if payable on demand the fair value is not materially different from the carrying value

# **Borrowing facilities**

The Company did not have an agreed bank borrowing facility at 30 June 2004.

# Currency risk

The Company does not hedge its exposure to exchange rate fluctuations.

#### (w) Acquisitions

On 26 July 2001 the Company acquired 440,000 ordinary shares of 1 pence each in e-phen Limited being 100 per cent. of its nominal share capital for a consideration including stamp duty of  $\pounds 17,688$ , satisfied by the issue of 440,000 ordinary shares of 1 pence each.

# (x) Post balance sheet events

On 6 December 2004, the share capital was sub-divided with each ordinary share of 1 pence being divided into 25 ordinary shares of 0.04p.

On 6 December 2004 £250,000 of amounts owing to EiRx Pharma Limited were satisfied by the issue of 6,250,000 ordinary shares at 4 pence per share to EiRx Pharma Limited.

On 6 December 2004, 17,745,011 ordinary shares were allotted at 2 pence per share in satisfaction of debts or loans of the Company to the Company's related parties.

Since the year end consultancy and other fees of £167,865 have been charged by related parties for services in the period. These fees are being satisfied as part of the share issue on 6 December 2004.

On 15 December 2004 the Company entered into a put and call option agreement with Billam plc and Billam AG (the "Put and Call Options") under which the Company had the right to require Billam AG and Billam plc equally to subscribe for up to 12,500,000 Ordinary Shares ("Call Option Shares") at the Placing Price. By the same agreement the Company granted to Billam plc and Billam AG an option each to subscribe for such number of Call Option Shares as have not been subscribed in relation to the call option. The Company reserved the right to pay the fee of £12,500 plus VAT due to Billam plc and Billam AG by the allotment and issue of Ordinary Shares at the Placing Price.

On 15 December 2004 the Company granted an option to HB-corporate, conditional upon Admission, to subscribe for such number of Ordinary Shares as are equal to 2 per cent. of the Enlarged Issued Share Capital ("HB Options").

On 15 December 2004 the Company entered into a placing agreement conditional, *inter alia*, upon Admission, with HB-corporate where it was agreed to place 37,500,000 Ordinary Shares of 0.04 pence at 2 pence per share on behalf of the Company. The admission of the Company to trading on AIM and the Placing are expected to take place on 20 December 2004.

Yours faithfully

GRANT THORNTON UK LLP

### PART V

### STATUTORY AND GENERAL INFORMATION

### 1. Responsibility

The Directors, whose names appear on page 4 of this document, accept individual and collective responsibility for the information contained in this document. To the best of the knowledge of the Directors (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 makes no omission likely to affect the import of such information.

# 2. Company and its share capital and subsidiary

- (a) The Company was incorporated on 30 May 2001 as Physiomics plc in England and Wales as a public limited company under the Act with registered number 4225086.
- (b) The principal legislation under which the Company operates is the Act and regulations made thereunder. The liability of members is limited.
- (c) The registered office of the Company and its principal place of business in the United Kingdom is The Magdalen Centre, Oxford Science Park, Robert Robinson Avenue, Oxford OX4 4GA.
- (d) At the date of this document the authorised and issued share capital of the Company is as follows:

	Authorised	Issued and fully		
	Number	£	paid Number	£
Ordinary Shares	25,000,000,000	10,000,000	191,845,911	76,738

(e) On the date of Admission (and following completion of the Placing), the authorised and issued share capital of the Company are expected to be as follows:

	Authorised	Issued and fully		
	Number	£	paid Number	£
Ordinary Shares	25,000,000,000	10,000,000	230,025,599	92,010

- (f) The Directors are generally and unconditionally authorised pursuant to section 80 of the Act to allot relevant securities up to an aggregate nominal value of £130,000 such authority (unless previously revoked or varied) to expire on the earlier of the next annual general meeting of the Company and 5 March 2006 save that the Company may before such expiry make an offer or agreement which would or might require relevant securities to be allotted after such expiry.
- (g) The provisions of section 89(1) of the Act which confer on Shareholders rights of pre-emption in respect of the allotment of securities which are, or are to be, paid up in cash (other than by way of allotment to employees under any employee share scheme as defined in section 743 of the Act) do not apply to the allotment of Ordinary Shares up to an aggregate nominal value of £190,000 until the earlier of the next annual general meeting of the Company and 5 March 2006 but would apply to any increase in the authorised share capital of the Company. Subject to certain limited exceptions, unless the approval of Shareholders in general meeting is obtained, the Company must normally offer Ordinary Shares to be issued for cash to existing Shareholders on a *pro rata* basis.
- (h) (i) On 15 December 2004 the Company granted an option to HB-corporate, conditional upon Admission, to subscribe for such number of Ordinary Shares as are equal to 2 per cent. of the Enlarged Issued Share Capital ("HB Options"). Further details of the agreement with HBcorporate granting the HB Options are set out in paragraph 5 of this Part V.
  - (ii) On 15 December 2004 the Company entered into a put and call option agreement with Billam plc and Billam AG (the "Put and Call Options") under which the Company had the right to require Billam AG and Billam plc equally to subscribe for up to 12,500,000 Ordinary Shares ("Call Option Shares") at the Placing Price. By the same agreement the Company granted to Billam plc and Billam AG an option each to subscribe for such number of Call Option Shares as have not been subscribed in relation to the call option. The Company reserved the right to pay the fee of £12,500 plus VAT due to Billam plc and Billam AG by the allotment and issue of Ordinary Shares at the Placing Price. Further details of the Put and Call Options are set out in paragraph 5

of this Part V. On 15 December 2004 the Company issued an aggregate of 679,688 Ordinary Shares to Billam AG and Billam plc in satisfaction of this fee.

- (i) Under the terms of the co-operation, licensing and marketing agreement between the Company and BTS, the Company granted an option ("BTS Option") to BTS to convert payments of £42,000 and €24,000 by BTS to the Company into Ordinary Shares at the Placing Price. Further details of the BTS Option are set out in paragraph 5 of this Part V.
- (j) No shares in 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.
- (k) Except as stated in this document:
  - (i) the Company does not have in issue any securities not representing share capital;
  - (ii) there are no outstanding convertible securities issued by the Company;
  - (iii) no share capital of the Company is under option or has been granted conditionally or unconditionally to be put under option;
  - (iv) the Company has no present intention to issue any of the authorised but unissued share capital of the Company; and
  - (v) none of the Directors nor members of their families (as such expression is defined in the AIM Rules) has a related financial product referenced to the Ordinary Shares.
- (l) e-phen was incorporated on 24 March 2000 in England and Wales as a private limited company under the Act with registered number 3955773. e-phen's registered office is The Magdalen Centre, Oxford Science Park, Robert Robinson Avenue, Oxford OX4 4GA. Its authorised share capital is £1,000,000 (divided into 100,000,000 ordinary shares of 1p each). Its issued share capital is £4,400 (divided into 440,000 ordinary shares of 1p each) and it is a non-trading wholly owned subsidiary of the Company.

#### **3.** Directors and their interests

(a) The directorships (other than of the Company) and partnerships held by each of the Directors at the date of this document and in the past five years preceding the date of this document are as follows:

#### **Stephen Parker**

Current Directorships Bannockton Limited sp<sup>2</sup> Consulting Limited White Light Therapy Limited Zeus Capital Limited

#### **David Collins**

Current Directorships Alford House (Management) Limited Eden Research Plc Fred Guy Limited Gieves Dormant 1 Limited Gieves Properties Limited Hayling Garages Limited Joseph Starkey Limited Newtons Restaurants Limited Oxford Capital Group Plc Spring Top Limited Winter Top Limited

**David Fell** *Current Directorships* None Previous Directorships Altium Capital Limited Oxford GlycoSciences Plc

#### Previous Directorships

Gieves Dormant 2 Limited Gieves Dormant 3 Limited Gieves Dormant 4 Limited Gieves Dormant 5 Limited Gieves Management Services Limited The Nucleus Housing Group Limited

*Previous Directorships* None

**Paul Harper** *Current Directorships* 

Angel Biotechnology Limited BioMedicon (sole trader) RegenTec Limited Sareum Limited Sareum Holdings Plc

#### John Pool

Current Directorships

EiRx Pharma Limited EiRx Therapeutics plc EiRx Therapeutics Limited (Ireland) Grannus Biotherapeutics Limited IDMOS plc **IDMOS** Dental Limited Inmexis Limited Innov8ive Detection and Monitoring Limited Nestech Limited The London Bioscience Innovation Centre Limited The Medical House plc Wellbeach Associates (a partnership) Wellbeach Limited Wrenoaks Limited Zyzygy plc

Previous Directorships Provensis Limited

#### Previous Directorships

Cellular Development Services Limited Envirag Limited Imseco Investments Limited Imseco Medical Services Limited London Capital Limited Meditrial Limited Technology Business Finance Limited

Current Directorships e-phen Limited

Previous Directorships Gerrard Limited Zetagen Limited

John Pool was a director of M2 Holdings Plc and its subsidiaries M2 Technology Limited and M2 Technology (Rentals) Limited each of which was placed in liquidation in 1998. All creditors were paid in full with Mr Pool satisfying all outstanding debts personally.

(b) None of the Directors has:

John Savin

- (i) any unspent convictions relating to indictable offences;
- (ii) had a bankruptcy order made against him or entered into any individual voluntary arrangements with its creditors;
- (iii) been a director of a company or limited liability partnership which has been placed in receivership, compulsory liquidation, creditors' voluntary liquidation or administration or entered into a company 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 at the time of or, within the 12 months preceding, such events;
- (iv) been a partner of a partnership which has been placed in compulsory liquidation or administration or which has entered into a partnership voluntary arrangement whilst he was a partner of that firm at the time of, or within twelve months preceding, such events;
- (v) had any asset belonging to him which has been the subject of a receivership or been a partner of a partnership whose assets have been placed in receivership whilst he was a partner at the time of, or within twelve months preceding, such receivership; or
- (vi) been publicly criticised by any statutory or regulatory authority (including any recognised professional body) or ever been disqualified by a court from acting as a director of a company or limited liability partnerships or from acting in the management or conduct of the affairs of any company or limited liability partnerships.
- (c) At the date of this document, the interests (all of which are beneficial unless otherwise stated) of the Directors in the share capital of the Company (as required to be notified to the Company pursuant to

section 324 to section 328 of the Act) are, as at the date of this document and as expected to be immediately following Admission, as follows:

	Current		As at date of Admission	
	Number of Ordinary Shares	Percentage of issued share capital held	Number of Ordinary Shares	Percentage of issued share capital held
Stephen Parker	Nil	Nil	Nil	Nil
John Savin	Nil	Nil	50,000	0.0%
David Collins	Nil	Nil	Nil	Nil
David Fell	Nil	Nil	300,000	0.1%
Paul Harper	Nil	Nil	Nil	Nil
John Pool	600,000	0.3%	600,000	0.3%

John Savin and David Fell hold respectively 1,251,110 and 35,929 ordinary shares of £1 each in the majority shareholder of the Company, EiRx Pharma, respectively representing approximately 8.7 per cent. and approximately 0.3 per cent. in the total issued share capital of EiRx Pharma. John Pool is a director and major shareholder in Wellbeach Limited which is the holder of the shares shown alongside Mr Pool's name.

Save as disclosed above none of the Directors has any interest whether beneficial or non beneficial in the share capital of the Company.

- (d) The following are particulars of the Directors' service agreements:
  - (i) Stephen Parker, Chairman

Dr Parker has entered into an executive service agreement with the Company dated 15 December 2004 effective from 24 March 2004 appointing him as part time Chairman of the Company. Dr Parker will be paid a basic annual salary of £36,000. The agreement is terminable by either party giving not less than 3 months' prior written notice to the other. The agreement contains rights in favour of the Company with regard to intellectual property rights and know-how developed or invented by Dr Parker, and also contains restrictive covenants given by Dr Parker.

(ii) John Savin, Chief Executive Officer

Dr Savin has entered into an executive service agreement with the Company dated 26 November 2004 effective from 26 July 2001 appointing him as Chief Executive Officer of the Company and superseding a prior service contract dated 26 July 2001. Dr Savin is paid a basic annual salary of £60,000 subject to review by the remuneration committee of the Board in June each year. Dr Savin will be paid an additional bonus linked to performance. The agreement is terminable by either party giving not less than 12 months' prior written notice to the other. The agreement contains rights in favour of the Company with regard to intellectual property rights and knowhow developed or invented by Dr Savin, and also contains restrictive covenants given by Dr Savin.

- (e) The following are particulars of Directors' letters of appointment:
  - (i) David Collins, Finance Director

By a letter of appointment dated 15 December 2004 with the Company, Mr Collins was appointed Finance Director of the Company effective from 28 May 2004. Mr Collins will be paid a basic fee of £1,000 per month payable monthly in arrears. The letter of appointment is terminable by either party giving to the other not less than three month's prior written notice.

(ii) David Fell, Science Director

By a letter of appointment dated 29 November 2004 with the Company, Professor Fell was appointed Non-executive Science Director of the Company effective from 30 June 2004. Professor Fell will be paid a fee of £750 per day up to a maximum of 20 days per year totalling in aggregate £15,000 per annum. The letter of appointment is terminable by either party giving to the other not less than one month's prior written notice.

# (iii) Paul Harper

By a letter of appointment dated 15 December 2004 with the Company, Dr Harper was appointed Non-executive Director of the Company effective from 24 September 2004. Dr Harper will be paid a fee of £12,000 per annum payable monthly in arrears. The letter of appointment terminable by either party giving to the other not less than one month's prior written notice.

(iv) John Pool

By a letter of appointment dated 15 December 2004 with the Company, Mr Pool was appointed Non-executive Director of the Company effective from 1 November 2004. Mr Pool will be paid a fee of  $\pounds$ 12,000 per annum payable monthly in arrears. The letter of appointment terminable by either party giving to the other not less than one month's prior written notice.

- (f) Other than as set out above, there have been no changes to Directors' service agreements or letters of appointment in the last six months.
- (g) It is estimated that the aggregate remuneration of the Directors (including benefits in kind and pension contributions) in the current financial year ending 30 June 2005 is expected to amount to £130,000 under arrangements in force at the date hereof. The aggregate remuneration (including benefits in kind and pension contributions) for the prior financial year of the Company being for the 12 months to 30 June 2004 was £57,000.
- (h) Save as referred to in paragraphs (d) and (e) above, there are no service agreements in existence between any of the Directors and the Company which cannot be determined by the Company without payment of compensation (other than statutory compensation) within one year.

#### Other interests

(i) At 14 December 2004 (the latest practicable date prior to the date of this document) and following Admission other than interests disclosed in paragraph (c) above, the Directors are aware of the following holdings which represent an interest (within the meaning of Part VI of the Act), directly or indirectly, jointly or severally, in three per cent., or more of the issued share capital of the Company:

	As at 14 Dec	As at 14 December 2004		y jollowing ssion
	Number of	Percentage of	Number of	Percentage of
	Ordinary	issued share	Ordinary	issued share
	Shares	capital held	Shares	capital held
EiRx Pharma	174,100,875	90.8%	174,100,875	75.7%
Peter Hoskins	11,420,500	6.0%	11,733,000	5.1%

Peter Hoskins' holding on the date of Admission includes 7,325,000 shares held by Billam AG, in which he has a controlling interest, and 1,000,000 shares held by his pension fund.

Save as disclosed above, the Company is not aware of any person who, immediately following Admission will, directly or indirectly, be interested in three per cent. or more of the issued share capital of the Company, or who, directly or indirectly, jointly or severally, exercises or could exercise control over the Company.

#### 4. Memorandum and Articles of Association

The principal object of the Company, which is set out in Clause 4 of its Memorandum of Association is a general commercial company.

The Articles of Association of the Company contain provisions, *inter alia*, to the following effect:

Votes of members

- (i) Subject to special rights or restrictions as to voting attached to any class of shares by or in accordance with the articles, at a general meeting every member present in person has on a show of hands one vote and every member present in person or by proxy has on a poll one vote for every share of which he is the holder.
- (ii) In the case of joint holders of a share, the vote of the senior who tenders a vote, whether in person or by proxy, shall be accepted to the exclusion of the vote or votes of the other joint holder or holders, and seniority is determined by the order in which the names of the holders stand in the register.

(iii) A member in respect of whom an order has been made by a court or official having jurisdiction (whether in the United Kingdom or elsewhere) that he is or may be suffering from mental disorder or is otherwise incapable of running his affairs may vote, whether on a show of hands or on a poll, by his guardian, receiver, curator bonis or other person authorised for that purpose and appointed by the court. A guardian, receiver, curator bonis or other authorised and appointed person may, on a poll, vote by proxy if evidence (to the satisfaction of the Board) of the authority of the person claiming to exercise the right to vote is received at the office (or at another place specified in accordance with the articles for the delivery or receipt of forms of appointment of a proxy) or in any other manner specified in the articles for the appointment of a proxy within the time limits prescribed by the articles for the appointment of a proxy for use at the meeting, adjourned meeting or poll at which the right to vote is to be exercised.

# Transfer of shares

Save for in the case of shares which have become participating securities for the purposes of the Uncertificated Securities Regulations 2001 ("CREST Regulations"), title to which may be transferred by means of a relevant system such as CREST without a written instruction, all transfers of shares must be effected by an instrument of transfer in writing in any usual form or in any other form approved by the Board. The instrument of transfer shall be executed by or on behalf of the transferor and, except in the case of fully paid shares, by or on behalf of the transferee. The Board may, in its absolute discretion and without giving any reason, refuse to register any transfer of certificated shares unless:

- (i) it is in respect of a share which is fully paid up;
- (ii) it is in respect of a share on which the Company has no lien;
- (iii) it is in respect of only one class of share;
- (iv) it is in favour of a single transferee or not more than four joint transferees;
- (v) it is duly stamped (if required); and
- (vi) it is lodged at the registered office together with the relevant share certificate(s) and such other evidence as the Board may reasonably require to show the right of the transferor to make the transfer provided that the Board may not exercise such discretion in such a way as to prevent dealing from taking place on an open and proper basis.

The Board may, in its absolute discretion and without giving any reason, refuse to register the transfer of an uncertificated share which is in favour of more than four persons jointly or in any other circumstances permitted by the CREST Regulations (subject to any relevant requirements of the London Stock Exchange). If the Board refuses to register a transfer it must, within two months after the date on which the transfer was lodged with the Company, send notice of the refusal to the transferee.

The registration of transfers may be suspended by the Board for any period (not exceeding 30 days) in any year.

### Failure to disclose interest in shares

If a member, or any other person appearing to be interested in shares held by that member, has been issued with a notice pursuant to section 212 of the Act and has failed in relation to any shares (the "Default Shares") to give the Company the information thereby required within the prescribed period from the date of the notice, the following sanctions shall apply:

- (i) the member shall not be entitled in respect of the Default Shares to be present or to vote (either in person or by representative or proxy) at any general meeting or at any separate meeting of the holders of any class of shares or on any poll; and
- (ii) where the Default Shares represent at least 0.25 per cent. in nominal value of the issued shares of their class:
  - (A) any dividend or other money payable in respect of the shares shall be withheld by the Company which shall not have any obligation to pay interest on it and the members shall not be entitled to elect to receive shares instead of a dividend; and
  - (B) no transfer, of any certificated Default Shares shall be registered unless:
    - (i) the member is not himself in default in supplying the information required; and

(ii) the member proves to the satisfaction of the Board that no person in default as regards supplying such information is interested in any of the shares which are the subject of the transfer.

The above sanctions shall also apply to any shares in the Company issued in respect of the Default Shares (whether on capitalisation, a rights issue or otherwise).

In respect of any Default Shares which are in uncertificated form the Board may by written notice require their holder to change them from uncertificated form into certificated form.

# Dividends

Subject to the provisions of the Act and of the articles, the Company may by ordinary resolution declare dividends, but no such dividends shall exceed the amount recommended by the Board. All dividends shall be apportioned and paid proportionately to the amounts paid up or credited as paid up (otherwise than in advance of calls) on the shares during any portion or portions of the period in respect of which the dividend is paid. Interim dividends may be paid provided that they appear to the Board to be justified by the profits available for distribution. Unless otherwise provided by the rights attached to any share, no dividends in respect of a share shall bear interest. The Board may, with the prior authority of an ordinary resolution of the Company, direct that payment of a dividend may be satisfied by the distribution of specific assets including Ordinary Shares in the Company or in any other company.

Any dividend unclaimed after a period of 12 years from its due date of payment shall (if the Board so resolves) be forfeited and cease to remain owing by the Company and shall thereafter belong to the Company absolutely.

#### Distribution of assets on liquidation

Subject to any rights or restrictions attached to any class of shares, on a winding-up of the Company, the surplus of assets available for distribution shall be divided among the members in proportion to the amounts paid on their respective shares at the commencement of the winding-up, or, with the sanction of an extraordinary resolution of the Company, be divided amongst the members *in specie* in such manner as shall be determined by the liquidator.

#### Changes in share capital

The Company may alter its share capital as follows:

- (i) it may by ordinary resolution increase its share capital, consolidate and divide all or any of its share capital into shares of larger amounts, cancel any shares which have not been taken or agreed to be taken by any person and sub-divide its shares or any of them into shares of smaller amounts;
- (ii) subject to any consent required by law and to any rights for the time being attached to any shares, it may by special resolution reduce its share capital, any capital redemption reserve, any share premium account or other undistributable reserve in any manner; and
- (iii) subject to the provisions of the Act and to any rights for the time being attached to any shares it may with the sanction of a special resolution enter into any contract for the purchase of its own shares.

#### Directors' interests in contracts

Save as provided below, a Director shall not vote on, or be counted in the quorum in relation to, any resolution of the Board or any committee of the Board in respect of any transaction or any proposal to which the Company is or is to be a party and in which he has any material interest or duty which conflicts with the interests of the Company. A Director shall be entitled to vote (and be counted in the quorum) in respect of any resolution at such meeting if his duty or interest arises only because the resolution relates to one of the following matters:

- (i) the giving to him of any guarantee, security or indemnity in respect of money lent or obligations incurred by him at the request of or for the benefit of the Company or any of its subsidiary undertakings;
- (ii) the giving to a third party of any guarantee, security or indemnity in respect of a debt or obligation of the Company or any of its subsidiary undertakings for which he himself has assumed responsibility in whole or in part, either alone or jointly with others, under a guarantee or indemnity or by the giving of security;

- (iii) where the Company or any of its subsidiary undertakings is offering securities in which offer the Director is or may be entitled to participate as a holder of securities or in the underwriting or subunderwriting of which the Director is to participate;
- (iv) relating to another company in which he and any persons connected with him do not to his knowledge hold an interest in shares (as that term is used in sections 198 to 211 of the Act) representing 1 per cent. or more of either any class of the equity share capital, or the voting rights in such company;
- (v) relating to an arrangement for the benefit of the employees of the company or any of its subsidiary undertakings which does not award him any privilege or benefit not generally awarded to the employees to whom such arrangement relates; or
- (vi) concerning insurance which the Company proposes to maintain or purchase for the benefit of Directors or for the benefit of persons including Directors.

A Director may not vote or be counted in the quorum on any resolution of the Board or committee of the Board concerning his own appointment as the holder of any office or place of profit with the Company or any company in which the Company is interested (including fixing or varying the terms of such appointment or its termination).

Where proposals are under consideration concerning the appointments (including fixing or varying the terms of the appointment) of two or more Directors, such proposals may be divided and a separate resolution considered in relation to each Director. In each case, each such Director (if not otherwise debarred from voting) is entitled to vote (and be counted in the quorum) in respect of each resolution except that resolution concerning his own appointment.

# Directors

Unless otherwise decided by the Company by ordinary resolution the aggregate fees which the Directors shall be entitled to receive for their services in the office of director shall be such amount as the Board decides. Such sum (unless otherwise directed by the resolution of the Company by which it is approved) shall be divided among the Directors in such proportions and in such manner as the Board may determine or, in default of such determination, equally.

All the Directors are entitled to be repaid all reasonable travelling, hotel and other expenses properly incurred by them in or about the performance of their duties as Directors. If by arrangement with the Board any Director performs any special duties or services outside their ordinary duties as a Director and not in his capacity as a holder of employment or executive office, he may be paid such reasonable additional remuneration which may be by a lump sum or by way of salary, commission, participation in profits or otherwise as the board may determine.

No Director is to retire from office pursuant to section 293 of the Act by reason of the fact that he has attained the age of 70 or any other age and section 293 of the Act does not apply to the Company.

# Borrowing powers

The Board may exercise all the powers of the Company to borrow money and to mortgage or charge all or any of its undertakings, property, assets (present or future) and uncalled capital and, subject to the provisions of the Act, to issue debentures and other securities whether outright or as collateral security for any debt, liability or obligation of the Company or any third party.

# Redemption of Shares and Variation of Rights

Subject to the Act and to the rights attached to existing shares:

- (a) shares may be issued on terms that they are to be redeemed or, at the option of the Company or the holder, are liable to be redeemed; and
- (b) the rights attached to a class of shares may be varied or abrogated (whether or not the Company is being wound up) either with the consent in writing of the holders of at least three-fourths of the nominal amount of the issued shares of that class or with the sanction of an extraordinary resolution passed at a separate meeting of the holders of the issued shares of that class validly held in accordance with article 68 of the articles and other relevant provisions of the articles.

The rights attached to a class of shares are not, unless otherwise expressly provided for in the rights attaching to those shares, deemed to be varied by the creation, allotment or issue of further shares ranking *pari passu* 

with or subsequent to them or by the purchase or redemption by the Company of its own shares in accordance with the Act and article 39 of the articles of the Company.

# Winding Up

On a voluntary winding up of the Company the liquidator may, on obtaining any sanction required by law, divide among the members in kind the whole or any part of the assets of the Company, whether or not the assets consist of property of one kind or of different kinds, and vest the whole or any part of the assets in trustees upon such trusts for the benefit of the Shareholders as he, with the like sanction, shall determine. For this purpose the liquidator may set the value he deems fair on a class or classes of property, and may determine on the basis of that valuation and in accordance with the then existing rights of Shareholders how the division is to be carried out between Shareholders or classes of Shareholders. The liquidator may not, however, distribute to a Shareholder without his consent an asset to which there is attached a liability or potential liability for the owner.

# 5. Material contracts

The following contracts have been entered into by the Group, otherwise than in the ordinary course of business, during the two years preceding the date of this document, and are or may be material:

# (a) Nominated Adviser Agreement

On 10 September 2004, the Company entered into an agreement with Grant Thornton Corporate Finance pursuant to which Grant Thornton Corporate Finance agreed to act as the Company's nominated adviser and to advise and assist the Company in respect of the AIM Rules. The agreement is terminable by either party on the giving to the other of 30 days' prior written notice. The agreement contains indemnities from the Company to Grant Thornton Corporate Finance.

# (b) Broker Engagement Letter

On 10 August 2004, the Company entered into an agreement with HB-corporate ("Broker Engagement Letter") pursuant to which HB-corporate agreed to act on behalf of the Company in relation to the Placing and use its reasonable endeavours to raise up to £1 million on behalf of the Company on the terms of the Placing Agreement (referred to below). Under the terms of the Broker Engagement Letter the Company agreed to pay to HB-corporate a fee of £20,000 plus VAT on Admission, a commission equal to 5 per cent. of the aggregate value of the Placing Shares (excluding those shares not procured by HB-corporate) calculated at the Placing Price and to grant options totalling 2 per cent. of the Enlarged Share Capital at the Placing Price for three years.

# (c) Broker Agreement

On 15 December 2004, the Company entered into an agreement with HB-corporate pursuant to which HB-corporate agreed to act as broker to the Company for the purposes of the AIM Rules for an annual fee of  $\pounds$ 12,000 plus VAT payable quarterly in advance. The Broker Agreement is for an initial period of 12 months from the date of the Broker Agreement and thereafter terminable by either party giving to the other not less than 90 days' prior written notice.

# (d) Broker Option Agreement

On 15 December 2004, the Company entered into an agreement with HB-corporate under which, subject to and conditional upon Admission, the Company granted to HB-corporate an option to subscribe at the Placing Price for Ordinary Shares representing 2 per cent. of the Enlarged Issued Share Capital. The options are exercisable by HB-corporate at any time from Admission for a period of three years.

# (e) Placing Agreement

On 15 December 2004, the Company entered into a conditional agreement with EiRx Pharma, HB-corporate and the Directors pursuant to which HB-corporate agreed to use its reasonable endeavours to procure placees, as agent for the Company, for 37,500,000 Placing Shares at the Placing Price. The Placing Agreement is conditional upon, *inter alia*, Admission occurring on or before 22 December 2004 (or such later date as the Company, EiRx Pharma and HB-corporate may agree), being not later than 31 December 2004. In consideration of its services in connection with the Placing, and subject to it becoming unconditional, the Company agreed to pay to HB-corporate (together with VAT where applicable) a broker fee of £20,000, a placing commission of 5 per cent. on the aggregate value of the Placing Shares (excluding those Placing Shares not directly procured by HB-corporate) at the Placing Price, an option over 2 per cent. of the

Enlarged Issued Share Capital and all professional fees incurred by HB-corporate in connection with the Placing.

The Placing Agreement contains warranties given by the Company, EiRx Pharma and the Directors in favour of HB-corporate as to, *inter alia*, the accuracy of information contained in this document and other matters relating to the Company, the Group and its business. In addition, the Company, EiRx Pharma and the Directors have given an indemnity to HB-corporate in respect of certain liabilities it may incur in respect of the Placing.

HB-corporate is entitled to terminate the Placing Agreement in specified circumstances prior to Admission, principally in the event of a material breach of the Placing Agreement or any of the warranties contained in it.

EiRx Pharma and the Directors have severally undertaken to the Company and to HB-corporate not to dispose of the Ordinary Shares held by each of them at or following Admission at any time up to the first anniversary of Admission.

# (f) Consent Agreement with Shareholders of EiRx Pharma

On 6 December 2004, the Company entered into an agreement with EiRx Pharma and certain of the shareholders in EiRx Pharma who constituted an Investor and Super Investor Majority of EiRx Pharma, who consented to the doing of all acts by the Company in connection with the Placing, Admission and matters related thereto and to receive warranties and assurances that the entry by the Company of the contracts and agreements referred to in the agreement did not constitute an infringement by EiRx Pharma of the terms of an agreement dated 1 August 2002 by and between the shareholders of EiRx Pharma.

# (g) Relationship Agreement

On 15 December 2004, EiRx Pharma entered into a relationship agreement with the Company conditional upon Admission, under the terms of which EiRx Pharma undertook to the Company not to exercise its voting rights and other powers of control available to it in relation to the Company whether such rights or powers arise through representation on the board or through its holding of shares in the Company (*inter alia*):

- (i) to alter the composition of the board in such a way that the majority of Directors thereon would not be regarded as being independent of EiRx Pharma;
- (ii) other than *bona fide* in the interest of the Company as a whole; and
- (iii) to enter into any contract or relationship with the Company whether legally binding or otherwise save where such contract or relationship is entered into in the ordinary and proper course of business and on an arms length and commercial basis.

In addition EiRx Pharma undertook to the Company to notify it if a business approach is made to it in relation to the Company, and further undertook not to compete with the Company in any business operated by the Company or any subsidiary of it.

The Relationship Agreement is expressed to continue until EiRx Pharma is no longer a controlling shareholder as defined in the Listing Rules of the UKLA.

# (h) BTS Option

On the terms of a co-operation licensing and marketing agreement between BTS and the Company dated 14 July 2004, *inter alia*, BTS paid to the Company in July 2004 the sums of £42,000 and €24,000. Under the terms of this agreement, until 31 December 2005, BTS has the right but not the obligation to treat such amounts as a subscription for Ordinary Shares at the price per share in the latest round of investment into the Company. If BTS does not exercise this option on the earlier of either Admission or 31 December 2005, the option will lapse. At the date of this document, the Company has not received any notice from BTS for the exercise of this option.

#### *(i) Consultancy Agreement*

On 26 July 2001, the Company entered into an agreement with Peter Hoskins for the provision by Mr Hoskins of certain consultancy services to the Company ("Consultancy Agreement"). Under the terms of Consultancy Agreement Peter Hoskins is payable a fee of £12,000 per annum payable by the Company monthly in arrears. This agreement is terminable on 12 months' notice by either the Company or Peter

Hoskins. With effect from 1 August 2002 until 31 December 2004 Peter Hoskins has agreed to waive his fees in respect of this Agreement but Peter Hoskins has reserved the right to require payment of his fees at any time from 1 January 2005 under the terms of the Consultancy Agreement.

# (*j*) Put and Call Option Agreement

On 15 December 2004, the Company entered into an agreement with Billam AG and Billam plc ("the Optionholders") pursuant to which the Optionholders granted to the Company an option ("Call Option") to require the Optionholders to subscribe for up to 12,500,000 Ordinary Shares ("Call Option Shares") at the Placing Price. The Call Option is exercisable by the Company for a period of 9 months commencing from 9 months following Admission (subject to receipt of 1 months prior written notice from the Company) ("Call Option Period"). The number of Ordinary Shares exercisable under the Call Option is reduced in the event that certain additional funds are received by the Company. Under the same agreement the Company to allot and issue the Call Option Shares less any Ordinary Shares exercised pursuant to the Call Option. The Put Option is exercisable by either Optionholders are entitled to a fee of £12,500 plus VAT in equal proportion to be satisfied by the allotment and issue at the option of the Company of Ordinary Shares at the Placing Price.

# (k) Indemnities

On 15 December 2004, the Company entered into agreements with each of the Directors and each of Billam AG, Peter Hoskins and EiRx Pharma ("the Indemnifiers"), pursuant to which the Indemnifiers agreed jointly and severally to indemnify the Directors for their personal liabilities under the Placing Agreement. The Company agreed to pay a fee to Billam AG for the provision of such indemnity to be agreed with Billam AG not exceeding in aggregate £10,000 within 60 days of Admission.

# 6. Litigation

No company in the Group is engaged in any litigation or arbitration and, so far as the Directors are aware, has no litigation or claim pending or threatened against it which has, has had or may have, a significant effect on the Company's financial position.

# 7. Group structure

At the date of this document the Company has one wholly owned subsidiary, e-phen.

# 8. Taxation

The following information is intended only as a general guide to the position under current United Kingdom law and Inland Revenue practice as at the date of this document for shareholders who are the beneficial owners of Ordinary Shares, resident or ordinarily resident in the United Kingdom for tax purposes and who hold their Ordinary Shares as an investment and is not a substitute for the investors obtaining professional advice before buying shares. Its applicability will depend upon the particular circumstances of individual shareholders. The summary is not exhaustive and does not generally consider tax reliefs or exemptions.

# (a) United Kingdom Residents

# (i) Taxation on chargeable gains

If a Shareholder disposes of all or any of the Ordinary Shares acquired under the Placing he or she may, depending on the Shareholder's particular circumstances, incur a liability to taxation on chargeable gains. Individuals, personal representatives and trustees may be entitled to taper relief. Companies which hold shares as investments may be entitled to an indexation allowance to reduce the gain chargeable.

# (ii) Stamp Duty and Stamp Duty Reserve Tax

Except in relation to certain categories of person, including market makes, brokers, dealers and persons connected with depository arrangements or clearance services, where special rules apply:

No stamp duty or stamp duty reserve tax will be payable on the issue of the Placing Shares;

The transfer or sale of Ordinary Shares will normally be subject to *ad valorem* stamp duty (rounded up to the nearest  $\pounds$ 5) at the rate of one-half of one per cent. of the consideration paid. However, if an unconditional agreement to transfer such shares is not completed by a duly stamped transfer, stamp duty reserve tax will be payable, normally at the rate of one-half of one per cent. of the consideration paid.

# (iii) Taxation of dividends and distributions

Under current United Kingdom tax legislation, no withholding tax will be deducted from dividends paid by the Company.

An individual Shareholder who is resident in the United Kingdom for tax purposes and who receives a dividend will be entitled to a tax credit in respect of the dividend and will be taxable on the aggregate of the net dividend received and the tax credit (such aggregate being the "gross dividend"). The value of the tax credit is currently one ninth of the net dividend (or 10 per cent. of the "gross dividend"). The gross dividend is treated as the top slice of such individual's income. An individual so resident who is not liable to income tax in respect of the gross dividend will not be able to claim repayment of the tax credit from the Inland Revenue.

In the case of an individual so resident who is not liable to income tax at a rate greater than the basic rate, the tax credit will discharge his liability to income tax in respect of the gross dividend and there will be no further tax to pay and no right to claim any repayment of the tax credit from the Inland Revenue. In the case of an individual so resident who is liable to income tax at the higher rate on dividends (currently 32.5 per cent.) the tax credit will be set against his tax liability in respect of the gross dividend and, accordingly, he will have to pay additional tax at the rate of 22.5 per cent., of the gross dividend, to the extent that the gross dividend falls above the threshold for higher rate income tax.

Subject to certain exceptions a shareholder which is a company resident in the United Kingdom for tax purposes will not be liable to United Kingdom corporation tax on any dividend received from the Company.

Trustees of discretionary trusts and of trusts where dividend income is accumulated are liable to tax at the rate of 32.5 per cent. of the gross dividend receipt. The tax credit of 10 per cent. will be set against the trustee's tax liability in respect of the gross dividend and accordingly the trustees will have to pay additional tax at the rate of 22.5 per cent. of the gross dividend. This is a complex area and trustees of such trusts should consult their own tax adviser,

# Non-United Kingdom Residents

Subject to certain exemptions for individuals who are Commonwealth citizens, citizens of the Republic of Ireland, residents of the Isle of Man of the Channel Islands, nationals of states which are part of the European Economic Area and certain others, the right of a Shareholder who is not a resident in the UK (for tax purposes) to claim any part of the tax credit will depend upon the existence and terms of any double taxation treaty between the UK and the country in which that person is resident. The tax credit is one ninth of the cash dividend paid. Persons who are not resident in the UK should consult their own tax advisers concerning their liabilities (in the UK and any other country) on dividends received, whether they are entitled to claim any part of the tax credit and if so, the procedure for doing so, and whether any double taxation relief is due in any country in which they are subject to tax.

Any person who is any doubt as to his or her tax position or who is subject to tax in a jurisdiction other than the United Kingdom should consult an appropriate professional adviser.

# 9. Working capital

The Directors are of the opinion that, having made due and careful enquiry and taking into account the net proceeds of the Placing and the facilities under the Put and Call Option Agreement described in paragraph 5 of this Part V, the working capital available to the Company and Group is sufficient for its present requirements, that is for at least 12 months from the date of Admission.

#### **10.** Intellectual property

In the opinion of the Directors based on the Company's present business model the following patents, intellectual property rights or contracts are or may be of fundamental importance to the Company's business:

- (a) US Patent 6,446,055;
- (b) the rights the Company has in or to the software and technology comprised in European Patent 0937286 in the UK, Ireland, France, Germany, Holland, Italy and Sweden;
- (c) the intellectual property rights the Company has in or to the software, technology and know-how developed by or on behalf of the Company based on and in addition to the patent and other rights the Company has under (a) and (b);

- (d) the trademark SystemCell<sup>TM</sup>;
- (e) the Contract dated 20 July 2004 between BTS and the Company; and
- (f) the Contract dated 11 August 2004 between Cronos Therapeutics Limited and the Company.

### 11. Miscellaneous

- (a) The total costs and expenses payable by the Company in connection with or incidental to Admission are estimated to amount to approximately £240,000 excluding VAT.
- (b) The financial information for the relevant accounting periods set out in the Accountant's Reports in Part IV of this document concerning the Company does not constitute statutory accounts of the Company within the meaning of section 240 of the Act.
- (c) The minimum amount which, in the opinion of the Directors, must be raised under the Placing to provide sums required to be provided in respect of the matters specified in paragraph 21(a) to Schedule I of the POS Regs is £750,000 which will be applied as set out below:

(i)	Purchase of property	£nil
(ii)	Expenses of the Placing (including commissions)	£0.24 million
(iii)	Repayment of borrowings in respect of(i) and (ii) above	£nil
(iv)	Working capital	£0.51 million

- (d) The following persons have received fees or securities of £10,000 or more in the previous 12 months:
  - (i) On 6 December 2004, EiRx Pharma was allotted and issued 6,250,000 Ordinary Shares by the Company at a price of 4p per share in satisfaction of advances made by EiRx Pharma to the Company of £250,000. EiRx Pharma is the majority shareholder in the Company.
  - (ii) On 6 December 2004, Peter Hoskins was allotted and issued 4,908,000 Ordinary Shares by the Company at a price of 2p per share in satisfaction of a loan of £56,160 owing by the Company in respect of funds advanced by Mr Hoskins and £42,000 owing in respect of management and consultancy services provided to the Company. Of these shares 1,000,000 such Ordinary Shares were issued to his pension fund, 500,000 were issued to Jemima Thorpe at the direction of Mr Hoskins.
  - (iii) On 6 December 2004, Billam AG, a company controlled by Mr Hoskins, was allotted and issued 7,012,500 Ordinary Shares by the Company at a price of 2p per share in satisfaction of a loan of £500 owing by the Company to Billam AG, £39,750 in respect of services provided by Billam AG to the Company and in consideration of the transfer to the Company of a debt owing by EiRx Pharma to Billam AG of £100,000 in respect of fees for management and consultancy services provided by Billam AG to EiRx Pharma.
  - (iv) On 6 December 2004, Billam plc was allotted and issued 5,224,511 Ordinary Shares by the Company at a price of 2p per share in satisfaction of a loan of £89,490.22 owing by the Company to Billam plc and £15,000 for management and consultancy services provided by Billam plc to the Company.
  - (v) On 6 December 2004, Wellbeach Limited (a company controlled by John Pool, a director of the Company), was allotted and issued 600,000 Ordinary Shares by the Company at a price of 2p per share in consideration of the transfer to the Company of a debt owing by EiRx Pharma to Wellbeach Limited of £12,000 in respect of fees for consultancy services provided by Wellbeach Limited to EiRx Pharma.

Save as disclosed above and in paragraph 5 of this Part V, no person (excluding professional advisers otherwise disclosed in this document and trade suppliers) has received directly or indirectly from the Company within the 12 months preceding the application for Admission to trading on AIM, being the latest practicable date prior to the date of this document or entered into contractual arrangements for (not otherwise disclosed in this document) to receive, directly or indirectly, from the Company on or after Admission any of the following: fees totalling  $\pounds 10,000$  or more, securities in the Company with a value of  $\pounds 10,000$  or more at the date of Admission.

(e) Save as disclosed, no exceptional factors have influenced the Company's activities.

- (f) The Company's accounting reference date is 30 June.
- (g) The Company has no significant investments in progress.
- (h) Grant Thornton UK LLP has given and not withdrawn its written consent to the issue of this document with its name included in it and with the inclusion therein of its reports and references thereto in the form and context in which they are included for the purpose of paragraph 13(1)(g) of the POS Regs and accepts responsibility for such report in accordance with paragraph 45(8)(b) of Schedule 1 to the POS Regs and have not become aware since the date of its report of any matter affecting the validity of such report at that date.
- (i) HB-corporate has given and not withdrawn its written consent to the issue of this document with the inclusion therein of references to its name in the form and context in which it appears.
- (j) Grant Thornton Corporate Finance has given and not withdrawn its written consent to the issue of this document with the inclusion therein of references to its name in the form and context in which it appears.
- Grant Thornton Corporate Finance has been appointed nominated adviser to the Company. Under the (k) AIM Rules the nominated adviser owes certain responsibilities to London Stock Exchange. In accordance with these rules, Grant Thornton Corporate Finance has confirmed to London Stock Exchange that it has satisfied itself that the Directors have received independent advice and guidance as to the nature of their responsibilities and obligations under the AIM Rules and that, to the best of its knowledge and belief, all relevant requirements of the AIM Rules (save for compliance with Regulation 9 of the POS Regulations in respect of which the nominated adviser is not required to satisfy itself) have been complied with. Grant Thornton Corporate Finance has also satisfied itself that the contents of this document have been appropriately verified. In giving its confirmation to the London Stock Exchange, Grant Thornton Corporate Finance has not made its own enquiries except as to matters which have come to its attention and on which it considered it necessary to satisfy itself. No liability whatsoever is accepted by Grant Thornton Corporate Finance or its advisers for the accuracy of any information or opinions contained in this document or for the omission of any material information, for which the Company and its Directors are solely responsible. Grant Thornton Corporate Finance does not regard itself as being, and is not, a "responsible person" (as that term is used in section 13 of the POS Regs) in relation to this document.
- (1) Save as set out in this document, there are no arrangements, nor are there intended to be any arrangements, for there to be dealings in the Ordinary Shares.
- (m) Save as disclosed above there has been no significant change in the financial or trading position of the Group since 30 June 2004 being the date to which the audited financial statements of the Company were prepared.

# 12. Availability of this document

Copies of this document will be available free of charge from the Company at its registered office between the hours of 9.00 a.m. and 5.00 p.m. Monday to Friday (excluding UK public holidays) for a period of not less than one month from the date of Admission.

Dated 15 December 2004

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