THIS DOCUMENT IS IMPORTANT AND REQUIRES YOUR IMMEDIATE ATTENTION. If you are in any doubt as to the contents of this document or what action you should take, you are recommended to seek your own financial advice immediately from an independent financial adviser who specialises in advising on shares or other securities and who is authorised under the Financial Services and Markets Act 2000, as amended (''FSMA'').

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

The Directors of the Company, whose names appear on page 8 of this document and the Company, accept responsibility, collectively and individually, for the information contained in this document. To the best of the knowledge of the Directors and the Company, having taken all reasonable care to ensure such is the case, the information contained in this document is in accordance with the facts and contains no omission likely to affect the import of such information. Applications will be made for the ordinary shares of 1.5p each in the Company (the ''**Ordinary Shares**''), issued and to be issued, and the Warrants, to be issued, pursuant to the Placing to be admitted to trading on the AIM market (''**AIM**'') of the London Stock Exchange plc (''**Admission**''). It is expected that Admission will become effective and that dealings in the Ordinary Shares and Warrants will commence at 8.00 a.m. on 26 February 2016.

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. Each AIM company is required pursuant to the AIM Rules for Companies to have a nominated adviser. The nominated adviser is required to make a declaration to the London Stock Exchange on Admission in the form set out in Schedule Two to the AIM Rules for Nominated Advisers. The London Stock Exchange has not itself examined or approved the contents of this document.

The whole of the text of this document should be read. You should be aware than an investment in the Company involves a high degree of risk. Your attention is drawn to the risk factors set out in Part 3 of this document.

Shield Therapeutics plc

(Incorporated in England and Wales with company no. 9761509 under the Companies Act 2006)

PLACING OF 21,666,662 ORDINARY SHARES AT 150p PER ORDINARY SHARE AND 7 WARRANTS FOR EVERY 13 PLACING SHARES AND ADMISSION TO TRADING ON AIM

Nominated Adviser and Sole Bookrunner

Liberum Capital Limited

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

Liberum Capital Limited (''**Liberum**''), authorised and regulated by the FCA in the United Kingdom, is acting exclusively for the Company and no one else in connection with the Institutional Placing and Admission, will not regard any other person as their respective customer or be responsible to any other person for providing the protections afforded to customers of Liberum, nor for providing advice in relation to this document, the Institutional Placing, Admission or any other transaction or arrangement referred to in this document. Its responsibilities as the Company's nominated adviser under the AIM Rules for Nominated Advisers are owed solely to the London Stock Exchange and are not, under the AIM Rules for Nominated Advisers, owed to the Company or to any Director or to any other person in respect of his or her decision to acquire Ordinary Shares in reliance on any part of this document. No representation or warranty, express or implied, is made by Liberum as to any of the contents of this document (without limiting the statutory rights of any person to whom this document is issued). No liability is accepted by Liberum for the accuracy of any information or

opinions contained in, or for the omission of any material information from, this document, for which the Company and the Directors are solely responsible.

This document does not constitute an offer to sell or a solicitation or offer to buy or subscribe for Ordinary Shares or Warrants unless permitted by applicable law and regulation. This document is not for distribution in the Prohibited Territories other than in compliance with the securities laws of the Prohibited Territories. The Ordinary Shares, the Warrants and any Ordinary Shares that may be issued pursuant to the exercise of Warrants have not been and will not be registered under the United States Securities Act of 1933 (as amended) or under the securities legislation of the Prohibited Territories or in any country, territory or possession where to do so would contravene local securities laws or regulations and the Ordinary Shares, the Warrants and any Ordinary Shares that may be issued pursuant to the exercise of Warrants may not be offered or sold directly or indirectly within the Prohibited Territories or to, or for the account of, or benefit of, any person within the Prohibited Territories other than in compliance with the securities laws of the Prohibited Territories. The distribution of this document in jurisdictions other than the United Kingdom may be restricted by law and therefore any person into whose possession this document comes should inform themselves about and observe any such restrictions. Any failure to comply with these restrictions may constitute a violation of the securities laws in any such jurisdictions.

The Ordinary Shares, the Warrants and any Ordinary Shares that may be issued pursuant to the exercise of Warrants may not be publicly offered, sold or advertised, directly or indirectly, in, into or from Switzerland and will not be listed on the SIX Swiss Exchange or on any other exchange or regulated trading facility in Switzerland. Neither this document nor any other offering or marketing material relating to the Ordinary Shares and Warrants constitutes a prospectus as such term is understood pursuant to article 652a or article 1156 of the Swiss Code of Obligations or a listing prospectus within the meaning of the listing rules of the SIX Swiss Exchange or any other regulated trading facility in Switzerland or a simplified prospectus as such term is defined in the Swiss Collective Investment Schemes Act, and neither this document nor any other offering or marketing material relating to the Ordinary Shares and Warrants may be publicly distributed or otherwise made publicly available in Switzerland.

FORWARD LOOKING STATEMENTS

This document includes statements that are, or may be deemed to be, ''forward-looking statements''. These forward-looking statements can be identified by the use of forward-looking terminology, including the terms ''believes'', ''estimates'', ''anticipates'', ''expects'', ''intends'', ''plans'', ''may'', ''will'' or ''should'' or, in each case, their negative or other variations or comparable terminology. All statements other than statements of historical fact included in this document are forward-looking statements. They appear in a number of places throughout this document and include statements regarding the Directors' or the Group's intentions, beliefs or current expectations concerning, among other things, its operating results, financial condition, prospects, growth, expansion plans, strategies, the industry in which the Group operates and the general economic outlook.

Forward-looking statements include, but are not limited to, statements about:

- the Company's plans to develop and commercialise its products;
- the Company's ongoing and planned clinical and non-clinical trials;
- the timing and the Company's ability to obtain and maintain regulatory approval for its products;
- the Company's estimates regarding expenses, future revenue, and future capital requirements;
- the Company's ability to expand the approved indications for its products;
- the Company's commercialisation, marketing and manufacturing capabilities and strategy;
- competition in the Company's industry;
- the performance of the Company's third-party suppliers and manufacturers;
- the Company's intellectual property position;
- the costs of compliance and the Company's ability to comply with new and existing governmental regulations; and
- the continued involvement of key members of management.

By their nature, forward-looking statements involve risks and uncertainties because they relate to events and depend on circumstances that may or may not occur in the future and therefore are based on current beliefs and expectations about future events. Forward-looking statements are not guarantees of future performance and the Group's actual operating results and financial condition, and the development of the industry in which it operates may differ materially from those made in or suggested by the forward-looking statements contained in this document. In addition, even if the Group's operating results, financial condition and liquidity, and the development of the industry in which the Group operates are consistent with the forward- looking statements contained in this document, those results or developments may not be indicative of results or developments in subsequent periods. Accordingly, prospective investors should not rely on these forward-looking statements.

Any forward-looking statements that the Group makes in this document speak only as of the date of the document, and none of the Company, the Directors or Liberum undertakes any obligation to update such statements unless required to do so by applicable law. Comparisons of results for current and any prior periods are not intended to express any future trends or indications of future performance, unless expressed as such, and should only be viewed as historical data.

FINANCIAL INFORMATION

Unless otherwise indicated, the financial information included in this document is based on International Financial Reporting Standards ("**IFRS**") and International Financial Reporting Standards Interpretations Committee interpretations as adopted by the European Union, and those parts of the Act applicable to the companies reporting under IFRS. IFRS, as adopted by the European Union, differs in certain aspects from International Financial Reporting Standards as issued by the International Accounting Standards Board.

The preparation of financial information in conformity with IFRS requires the use of certain critical accounting estimates. It also requires management to exercise its judgment in the process of applying the Company's accounting policies. The areas involving a higher degree of judgment or complexity, or areas where assumptions and estimates are significant to the consolidated financial information, are disclosed in the notes to the financial information set out in Part 5 (*Historical Financial Information for Shield Holdings*) and Part 6 (*Historical Financial Information for Phosphate Therapeutics*).

The Company's financial year runs from 1 January to 31 December. The financial information included in this document is not intended to comply with the applicable accounting requirements of the Securities Act and the related rules and regulations that would apply if the Ordinary Shares, the Warrants or any Ordinary Shares that may be issued pursuant to the Warrants, were to be registered in the United States. Compliance with such requirements would require the modification or exclusion of certain information included in this document and the presentation of certain information which is not included in this document.

The financial information presented in this document was not prepared in accordance with U.S. Generally Accepted Accounting Principles ("**U.S. GAAP**") or audited in accordance with U.S. Generally Accepted Auditing Standards ("**U.S. GAAS**") or the standards of the Public Company Accounting Oversight Board ("**PCAOB Standards**"). No opinion or any other assurance with regard to any financial information was expressed under U.S. GAAP, U.S. GAAS or PCAOB Standards and the financial information is not intended to comply with SEC reporting requirements. Compliance with such requirements would require the modification, reformulation or exclusion of certain financial measures. In addition, changes would be required in the presentation of certain other information. In particular, no reconciliation to U.S. GAAP is provided.

Rounding

Percentages and certain amounts included in this document have been rounded for ease of presentation. Accordingly, figures shown as totals in certain tables may not be the precise sum of the figures that precede them.

Currencies

Unless otherwise indicated, in this document, all references to:

- pounds sterling or £ are to the lawful currency of the United Kingdom;
- U.S. dollars or U.S.$ are to the lawful currency of the United States;

- Swiss francs or Fr are to the lawful currency of Switzerland; and
- euro or € are to the lawful currency of the European Union (as adopted by certain member states).

Unless otherwise indicated, the financial information contained in this document has been expressed in pounds sterling. For all members of the Group in the United Kingdom, the functional currency is pounds sterling and the Group presents its financial statements in pounds sterling.

The basis of translation of foreign currency transactions and amounts in the financial information set out in Part 5 (*Historical Financial Information for Shield Holdings*) and Part 6 (*Historical Financial Information for Phosphate Therapeutics*) is described in those Parts. Information derived from this financial information set out elsewhere in this document has been translated on the same basis.

MARKET INFORMATION AND INDUSTRY DATA

This document includes market share, industry and scientific data and forecasts that the Company has obtained from industry publications, surveys and internal company sources. As noted in this document, the Company has obtained market and industry data relating to the Group's business from providers of industry data, including:

- World Health Organization
- GfK UK Limited

Scientific publications

This document includes scientific data from the following publications:

- Avni T, Bieber A, Steinmetz T, Leibovici L, Gafter-Gvili A. Treatment of Anemia in Inflammatory Bowel Disease – Systematic Review and Meta-Analysis, 2013, DOI: 10.1371/journal.pone.0075540.
- B. Benoist, E. McLean, I. Egli, and M. Cogswell, Worldwide Prevalence of Anaemia 1993-2005: WHO Global Database on Anaemia, WHO, Geneva, Switzerland, 2008.
- Chazot C and Jean G. The advantages and challenges of increasing the duration and frequency of maintenance dialysis sessions. Nature Clinical Practice Nephrology (2008) 5, 34-44. doi:10.1038/ncpneph0979.
- Dignass AU et al. European Consensus on the Diagnosis and Management of Iron Deficiency and Anaemia in Inflammatory Bowel Disease. J Crohn's and Colitis, 2015, 1-12.
- Ebner N., von Haehling S. Iron deficiency in heart failure: A practical guide. Nutrients. 2013;5:3730-3739. doi: 10.3390/nu5093730.
- Emmett M. A comparison of calcium-based phosphorus binders for patients with chronic kidney disease. Dialysis & Transplantation, 2006.
- Fishbane S, Pollack S, Feldman H, Joffe M Iron indices in chronic kidney disease in the National Health and Nutritional Examination Survey 1988-2004, Clin J Am Soc Nephrol 2009.
- Gasche C et al. 2014. Correcting Iron Deficiency Anaemia in IBD: A Pivotal Phase 3 Study of a Novel Oral Ferric Iron; Gasche C et al. 2014. Inflammatory Bowel disease.
- Growth Industry https://www.diabetes.org.uk/upload/Professional%20members%20area/Diabetes%20Upate/Winter%202010/Growthindustry_new.pdf Accessed September 2010.
- Iron deficiency anaemia: Assessment, prevention and control, World Health Organization, 2001.
- Kendrick J, Kestenbaum B and Chonchol M. Phosphate and Cardiovascular Disease. Adv Chronic Kidney Dis. 2011 March; 18(2): 113-119. doi: 10.1053/j.ackd.2010.12.003.
- Lindgren S, Wikman O, Befrits R, Blom H, Eriksson A, Granno C, et al. Intravenous iron sucrose is superior to oral iron sulphate for correcting anaemia and restoring iron stores in IBD patients: a randomized, controlled, evaluator-blind, multicentre study. Scand J Gastroenterol 2009:1-8.
- M. Aapro, A. Österborg, P. Gascón, H. Ludwig, Y. Beguin. Prevalence and management of cancer-related anaemia, iron deficiency and the specific role of i.v. iron, Annals of Oncology, 2012, 1954-1962, DOI: 10.1093/annonc/mds112.

- Patel K.V. Epidemiology of anemia in older adults. Semin Hematol. 2008;45(4):210-217.
- Pizzi R. Global Dialysis Industry Growing Despite Recession. Health Care Finance News, 2009.
- Powell, J, Bruggraber, S, Faria, N, Poots, LK, Hondow, N, Pennycook, TJ, Latunde-Dada, G, Simpson, R, Brown, AP & Pereira, DIA 2014, 'A nano-disperse ferritin-core mimetic that efficiently corrects anemia without luminal iron redox activity' Nanomedicine., 10.1016/j.nano.2013.12.011
- Tolkien Z, Stecher L, Mander AP, Pereira DI, Powell JJ. Ferrous sulphate supplementation causes significant gastrointestinal side-effects in adults: a systematic review and meta-analysis. PLoS One. 2015 Feb 20;10(2).
- Wilson A, Reyes E, Ofman J. Prevalence and outcomes of anaemia in inflammatory bowel disease: a systemic review of the literature, Am J Med 2004.

Third party reports

The Company has commissioned Stratagem and GfK to produce reports, copies of which can be found in Part 7 (*Patent Agent's Report*) and Part 8 (*Market Report*) of this document.

All other sources referenced in this document are publicly available or historically commissioned reports, and are not expert reports. The Company has not independently verified any of the data from third-party sources nor has it ascertained the underlying economic assumptions relied upon therein. Statements or estimates as to the Group's market position, which are not attributed to independent sources, are based on market data or internal information currently available to the Company. The Company confirms that information sourced from third parties has been accurately reproduced and, as far as the Company is aware and is able to ascertain from information published from third parties, no facts have been omitted which would render the reproduced information inaccurate or misleading. Estimates extrapolated from this data involve risks and uncertainties and are subject to change based on various factors, including those discussed in Part 3 (*Risk Factors*).

INFORMATION NOT CONTAINED IN THIS DOCUMENT

The contents of the Group's websites do not form any part of this document.

No person has been authorised to give any information or make any representation other than those contained in this document and, if given or made, such information or representation must not be relied upon as having been so authorised. Neither the delivery of this document nor any subscription made hereunder shall, under any circumstances, create any implication that there has been no change in the affairs of the Company since the date of this document or that the information in this document is correct as of any time subsequent to the date hereof.

Certain terms used in this document are defined, and certain technical and other terms used in this document are explained, in the Definitions and Glossary.

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EXPECTED TIMETABLE

Publication of this document	12 February 2016
Admission and dealings in the Ordinary Shares and Warrants to commence on AIM	8.00 a.m. on 26 February 2016
CREST accounts credited in respect of the New Shares and the Warrants	8.00 a.m. on 26 February 2016
Despatch of definitive share and warrant certificates (where applicable)	by 11 March 2016

Times set out in the timetable above that fall after the date of this document are indicative only and may be subject to change without further notice.

All references to time are to London time.

PLACING STATISTICS

Placing Price per Placing Share	150p
Number of existing Ordinary Shares in issue immediately prior to Admission	45,994,060
Number of New Shares to be issued by the Company upon Admission pursuant to the Corporate Reorganisation	40,474,694
Number of New Shares to be issued by the Company pursuant to the Placing	21,666,662
Number of Ordinary Shares in issue immediately following Admission	108,135,416
Number of Warrants in issue immediately following Admission	11,666,658
Placing Shares as a percentage of the enlarged issued ordinary share capital upon Admission	20%
Number of Ordinary Shares issuable by exercise of Warrants as a percentage of the enlarged issued ordinary share capital upon Admission	10.8%
Estimated net proceeds of the Placing receivable by the Company	£30.1 million
Market capitalisation of the Company at the Placing Price upon Admission	£162.2 million

DIRECTORS, SECRETARY AND ADVISERS

Directors	Dr Andrew Heath, Non-executive Chairman Carl Sterritt, Chief Executive Officer Richard CM Jones ACA, Chief Financial Officer James Karis, Non-executive Director Peter Llewellyn-Davies, Non-executive Director
Company Secretary	Richard CM Jones ACA
Registered Office	Northern Design Centre Baltic Business Quarter Gateshead Quays NE8 3DF
Nominated Adviser and Sole Bookrunner	Liberum Capital Limited Ropemaker Place 25 Ropemaker Street London EC2Y 9LY
Legal Adviser to the Company – English law	Stephenson Harwood LLP 1 Finsbury Circus London EC2M 7SH
Legal Adviser to the Company – US law	Waller Lansden Dortch & Davis, LLP 511 Union Street Suite 2700 Nashville TN 37219 USA
Legal Adviser to the Nominated Adviser as to English law and US law	Travers Smith LLP 10 Snow Hill London EC1A 2AL
Auditors and Reporting Accountants	KPMG LLP 1 Snowhill Snow Hill Queensway Birmingham B4 6GH
Tax Advisers	Ernst and Young LLP City Gate, St James' Blvd, Newcastle upon Tyne Tyne and Wear NE1 4JD
Registrar	Capita Registrars Limited The Registry 34 Beckenham Road Beckenham Kent BR3 4TU
Public Relations adviser to the Company	Consilium Strategic Communications Limited 41 Lothbury London EC2R 7HG

DEFINITIONS AND GLOSSARY

The following words and expressions shall have the following meanings in this document unless the context otherwise requires:

505b(2)	an NDA which is based on existing public data which was not generated by the applicant
Act	the Companies Act 2006, as amended from time to time
Admission	the admission of the Ordinary Shares and the Warrants to trading on the AIM market of the London Stock Exchange becoming effective
Admission Document	this document dated 12 February 2016
Adverse Event (AE)	any untoward medical occurrence associated with the use of a drug in humans whether or not considered drug related
AIM	AIM, a market operated by the London Stock Exchange
AIM Rules for Companies	the rules for companies whose securities are admitted to trading on AIM as published by the London Stock Exchange from time to time
AIM Rules for Nominated Advisers	the rules setting out the eligibility, ongoing obligations and certain disciplinary matters in relation to nominated advisers, as published by the London Stock Exchange from time to time
AMNOG	the Arzneimittelmarkt-Neuordnungsgesetz (or Pharmaceuticals Market Reorganisation Act), a German law relating to the marketing of pharmaceutical products in Germany
AOP Pharma	AOP Orphan Pharmaceuticals AG, a company incorporated in Austria
Articles	the articles of association of the Company
Audit Committee	the audit committee of the Board
Board	the board of directors of the Company from time to time
Business Day	a day (excluding Saturdays and Sundays or public holidays in England and Wales) on which banks generally are open for business in London for the transaction of normal business
Capital Distribution	means any dividend, distribution or other payment made by the Company, whether in cash, securities of the Company or property or assets of the Company (a "**Distribution**") but only if and to the extent that the Board characterises such Distribution as a return or distribution of capital by the Company
Centralised Procedure	a procedure that allows applicants to obtain a marketing authorisation that, once granted, is valid throughout the EU
Chairman	Dr Andrew Heath
CHMP	Committee for Medicinal Products for Human Use
Chronic Kidney Disease (CKD)	kidney damage for greater than 3 months, as defined by structural or functional abnormalities of the kidney
City Code	the City Code on Takeovers and Mergers
Company	Shield Therapeutics plc, a company incorporated in England and Wales under company number 09761507
CMC	Chemistry Manufacturing and Controls
Corporate Reorganisation	the arrangements described in paragraph 2 of Part 10 (*Additional Information*)
CREST	the relevant system as defined in the CREST Regulations in respect of which Euroclear is the operator (as defined in the CREST Regulations) in accordance with which securities may be held in uncertificated form

CREST Regulations	the Uncertificated Securities Regulations 2001 (SI 2001 No. 2001/3755) and any modification thereof or any regulations in substitution therefor for the time being in force
Current Market Price	means, with respect to an Ordinary Share at a particular date, the arithmetic average VWAP of an Ordinary Share for the five consecutive Trading Days ending on the Trading Day immediately preceding such date
DD-CKD	dialysis dependent CKD
Directors	the Executive and Non-Executive Directors of the Company
Disclosure and Transparency Rules	the disclosure and transparency rules made by the FCA under Part VI of FSMA
Distribution Agreement	the distribution agreement between ITH and AOP Pharma, further details of which are contained in paragraph 9.2 of Part 10 (*Additional Information*)
Drug Product (DP)	a finished form of therapeutic agent
Drug Substance (DS)	the central active ingredient in a pharmaceutical (formerly known as API)
ECCO	European Crohn's and Colitis Organisation
EEA	the European Economic Area
EMA	the European Medicine Agency
Employee Incentive Schemes	the Shield Therapeutics plc Long Term Incentive Plan and the Shield Therapeutics plc Company Share Option Plan, details of which are set out in paragraphs 8.1 and 8.2 of Part 10 (*Additional Information*) of this document
EU	the European Union
Euroclear	Euroclear UK & Ireland Limited
Executive Directors	Carl Sterritt and Richard CM Jones
FATCA	the US Foreign Account Tax Compliance Act
FCA	the Financial Conduct Authority
FDA	U.S. Food and Drug Administration
Ferritin	ubiquitous intracellular protein that stores iron and releases it in a controlled fashion
FSMA	the UK Financial Services and Markets Act 2000, as amended
Galenica or Galencia Limited	Galencia Limited, a company incorporated in Switzerland
Gastrointestinal (GI)	of or relating to both the stomach and the intestines
Gastrointestinal Symptom Rating Scale (GSRS)	a clinical rating scale for gastrointestinal symptoms in patients with irritable bowel syndrome and peptic ulcer disease
Generally Recognized as Safe (GRAS)	a status level assigned by the FDA to substances not known to be hazardous to health and thus approved for use in foods
GfK	GfK UK limited of 25 Canada Square, Canary Wharf, London, E14 5LQ, who have been appointed as market report providers to the Company
Good Clinical Practice (GCP)	an international ethical and scientific standard for the design, conduct and record of research involving humans
Good Manufacturing Practice (GMP)	good manufacturing practice in conformity with the relevant regulatory guidelines for the manufacturing of pharmaceuticals
Group	the Company, SHG and PTL and their subsidiaries and subsidiary undertakings
Haemoglobin (Hb)	the oxygen-carrying pigment and predominant protein in the red blood cells

HMRC	HM Revenue & Customs
Hyperphosphatemia	a condition in which a patient suffers from abnormally elevated levels of phosphate in the blood
IND	Investigational New Drug
Inflammatory Bowel Disease (IBD)	a disease that involves chronic inflammation of all or part of the digestive tract
Institutional Placing	means the offer of Placing Shares to certain existing Shareholders, institutional and other prospective investors as described in paragraph 13.1 of Part 10 (*Additional Information*) of this document
Intent-to-treat (ITT)	an analysis that includes all randomized patients in the groups to which they were randomly assigned, regardless of their adherence with the entry criteria, regardless of the treatment they actually received, and regardless of subsequent withdrawal from treatment or deviation from the protocol
Intravenous (IV)	a solution administered directly into the venous circulation via a syringe or intravenous catheter
Inventages	Inventages Whealth Management Inc., as General Partner of W. Health L.P.
Iron Deficiency (ID)	a condition resulting from too little iron in the body
Iron Deficiency Anaemia (IDA)	a condition where a lack of iron in the body leads to a reduction in the number of red blood cells
IRORPH	IRORPH GmbH, a company registered in Austria
IRORPH Top-up Option	the option described in paragraph 9.9 of Part 10 (Additional Information)
IRS	the U.S. Internal Revenue Service
ITH	Iron Therapeutics Holdings AG, a company registered in Switzerland with company number CH-114.810.684
Keryx	Keryx Biopharmaceuticals, Inc.
KDOQI	National Kidney Foundation Disease Outcomes Quality Initiative
Liberum	Liberum Capital Limited of Ropemaker Place, 25 Ropemaker Street, London, EC2Y 9LY
Lock-up Agreements	the lock-up agreements entered into between the Company, the Locked-up Shareholders and Liberum dated 12 February 2016 and described in paragraph 9.12 of Part 10 (*Additional Information*)
Locked-up Shareholders	Carl Sterritt, Andrew Heath, Richard CM Jones, Christian Schweiger, W. Health and IRORPH
London Stock Exchange	London Stock Exchange plc
MAA	marketing authorisation application
Member State	the member states of the European Economic Area.
Money Laundering Regulations	the Money Laundering Regulations 2007, as amended
MRC	the Medical Research Counsel in the UK
MRC Licence	the licence agreement entered into between PTL and the MRC on 22 December 2011 further details of which are contained in paragraph 9.1 of Part 10 (*Additional Information*)
NCE	New Chemical Entity
New Shares	the 62,141,356 new Ordinary Shares to be issued by the Company upon Admission comprising the 21,666,662 new Ordinary Shares to be issued pursuant to the Placing and

	40,474,694 new Ordinary Shares to be issued pursuant to completion of the Corporate Reorganisation
NDA	New Drug Application, by which a company proposes that the FDA approves a new pharmaceutical for sale and marketing in the US
NICE	National Institute for Health and Care Excellence (UK)
Nomination Committee	the nomination committee of the Board
Non-executive Directors	Dr Andrew Heath, James Karis and Peter Llewellyn-Davies
Official List	the official list maintained by the UK Listing Authority
Oral Ferrous Products (OFP)	oral ferrous iron supplementation product
Ordinary Shares	ordinary shares of nominal value 1.5p each in the capital of the Company
Pharmacokinetics (PK)	the branch of pharmacology concerned with the movement of the drugs within the body
Phase 3 Study	the pivotal safety and efficacy study which was conducted in 128 patients (64 to treatment and 64 to placebo) to compare Feraccru to placebo in two separate arms, Ulcerative Colitis and Crohn's disease
Piramal	Piramal Healthcare UK Limited, a wholly owned subsidiary of Mumbai – headquartered Piramal Enterprises Limited, a diversified conglomerate with operations in over 30 countries
Placing	the offer of Placing Shares and Warrants to certain existing Shareholders, institutional and other prospective investors pursuant to the Institutional Placing and Subscription as described in this document
Placing Agreement	the placing agreement entered into between the Company, the Directors and Liberum dated 12 February 2016 as summarised in paragraph 9.13 of Part 10 (*Additional Information*) of this document
Placing Price	150p per Placing Share
Placing Shares	the 20,226,665 New Shares to be issued by the Company pursuant to the Institutional Placing and the 1,439,997 New Shares to be issued by the Company pursuant to the Subscription
Prohibited Territories	the United States, Australia, Canada, The Republic of South Africa and Japan
Prospectus Directive	Directive 2003/71/EC of the European Parliament and of the Council of the European Union and any relevant implementing measure in each Relevant Member States
Prospectus Rules	the rules and regulations made by the FCA under Part VI of FSMA
PTL or Phosphate Therapeutics	Phosphate Therapeutics Limited, a company incorporated in England and Wales under company number 07618820, being a wholly owned subsidiary of the Company
QIB	''qualified institutional buyer'' as defined under Rule 144A
Register	the register of members of the Company
Registrar	Capita Registrars Limited
Regulation S	Regulation S under the Securities Act
Relationship Agreement	the relationship agreement between W. Health and the Company dated 12 February 2016 as summarised in paragraph 11 of Part 1 (*Key Information and details of the Placing*) of this document

Relevant Electronic System	means the computer-based system, and procedures, which enable title to units of a security to be evidenced and transferred without a written instrument
Remuneration Committee	the remuneration committee of the Board
Reorganisation Agreements	the agreement between the Company and PTL to acquire 100% of the share capital in PTL described in paragraph 9.10 of Part 10 (*Additional Information*) of this document, the W. Health Replacement Option and the IRORPH Top-up Option
Rule 144A	Rule 144A under the Securities Act
SDRT	stamp duty reserve tax
Scheme	means a scheme of arrangement under s.899 of the Act between the Company and holders of its Ordinary Shares pursuant to which all or the majority of the Ordinary Shares become vested in a third party
SEC	the U.S. Securities and Exchange Commission
Securities Act	the United States Securities Act of 1933, as amended
Senior Management	Paul Steckler, Kate Hopkinson, Jackie Mitchell, David Childs, Karen Nugent, Mark Simpson and Angela Hildreth
Shareholder	a holder of Ordinary Shares
SHG Group	Shield Holdings AG and its subsidiary undertakings
SHG	Shield Holdings AG, a company incorporated in Switzerland
Special Dividend	means, as determined by an investment bank of international repute, (i) any payment by the Company to holders of Ordinary Shares that the Company announces will be an extraordinary or special dividend; or (ii) any other ''special'' cash or non-cash dividend on, or distribution with respect to, the Ordinary Shares which is, by its terms or declared intent, declared and paid outside the normal operations or normal dividend procedures of the Company
Stratagem	Stratagem IPM Limited
Subscription	means the proposed subscription for Placing Shares by certain existing shareholders and other investors as summarised in paragraph 13.2 of Part 10 (*Additional Information*) of this document
Subscription Agreements	means the subscription agreements entered into by certain existing Shareholders and other investors dated 12 February 2016 as summarised in paragraph 9.14 of Part 10 (*Additional Information*) of this document
Summary of Product Characteristics (SmPC)	legal document approved as part of the MAA that contains the basis of information for healthcare professional on how to use the medicine)
Takeover Code	the City Code on Takeovers and Mergers
Takeover Offer	means a takeover offer within the meaning of s.974 of the Act
Trading Day	means any day on which the Ordinary Shares may be traded on AIM
Transferrin Saturation (TSAT)	a laboratory value of the ratio of serum iron and total iron-binding capacity in a person's body
United Kingdom or UK	the United Kingdom of Great Britain and Northern Ireland
UK Corporate Governance Code	the UK Corporate Governance Code as published by the Financial Reporting Council from time-to-time
UK GAAP	the generally accepted accounting principles currently adopted in the UK

UK Listing Authority or UKLA	the FCA acting in its capacity as the competent authority for the purposes of admission to the Official List
Uncertificated or in Uncertificated Form	an Ordinary Share or Warrant recorded on the Register as being held in uncertificated form in CREST and title to which, by virtue of the CREST Regulations, may be transferred by means of CREST
United European Gastroenterology Week (UEGW)	the premier venue for researchers across the globe to present their latest research on gastroenterology
United States or U.S.	the United States of America, its territories and possessions, any state of the United States of America and the District of Columbia
Vitra APA	the asset purchase agreement between ITH and Vitra Pharmaceuticals described in paragraph 9.3 of Part 10 (*Additional information*) of this document.
Vitra Pharmaceuticals	Vitra Pharmaceuticals Ltd, a company registered in England and Wales with company number 02791162
VWAP	means in relation to a Trading Day, the volume weighted average price (in pounds sterling, rounded to four decimal places) of the Ordinary Shares traded in the ordinary course of business on AIM on that Trading Day
WAKS	WAKS Privatstiftung, the parent of IRORPH
Warrants	the 11,666,658 warrants to subscribe for Ordinary Shares to be issued pursuant to the Placing, the particulars of which appear in Part 9 (*Particulars of Warrants*) of this document
W. Health	W. Health L.P. of Winterbotham Place, Marlborough & Queen Streets, PO Box N-3026, Nassau, Bahamas, an investment vehicle of Inventages
W. Health Replacement Option	the option described in paragraph 9.8 of Part 10 (*Additional Information*)

PART 1

KEY INFORMATION AND DETAILS OF THE PLACING

The following is a brief summary only and should be read in conjunction with the more detailed information and financial data and statements and risk factors appearing elsewhere in this document.

Prospective investors should read the whole of this document and not rely solely on the summarised information set out below:

1 Information of the Company and the Group

Shield Therapeutics is a specialty pharmaceutical company focused on the development and commercialisation of secondary care-focused pharmaceuticals.

The Company's key products are Feraccru and PT20, two late-stage pharmaceuticals for the treatment of iron deficiency anaemia and systemic phosphate accumulation (otherwise known as hyperphosphatemia), respectively.

Feraccru is a novel and effective oral ferric iron-based pharmaceutical product that the CHMP has given a unanimous positive opinion should be granted a marketing authorisation in all member states of the European Union. This marketing authorisation is scheduled to be issued in the first quarter of 2016. Initially Feraccru will be licensed to treat iron deficiency anaemia ("IDA") in patients with inflammatory bowel disease ("IBD"). A phased roll-out of commercialisation of Feraccru is expected to commence within the EU during 2016 targeted to treat IBD patients who have failed treatment on Oral Ferrous Products ("OFPs") or for whom such treatment is unsuitable. The Directors believe Feraccru has an achievable global peak annual sales opportunity in excess of £500 million.

PT20 is a novel iron-based phosphate binder being developed for the treatment of hyperphosphatemia related to chronic kidney disease ("CKD"). The product has completed Phase 2 clinical trials, having recently met all primary and secondary endpoints of a phase 2b pivotal study. It is anticipated that PT20 will be required to undergo one further pivotal study before a marketing authorisation application can be filed in major pharmaceutical markets.

2 Key strengths

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

(a) Near term revenue potential;

(b) Late stage assets that have either been approved or have delivered proof of concept;

(c) Large market opportunities with unmet needs;

(d) Experienced management team with extensive expertise;

(e) Opportunity to create operational leverage across the product portfolio;

(f) Strong intellectual property protection; and

(g) Attractive financial profile.

Further details of the key strengths are outlined in paragraph 3 of Part 2 (*Information on the Company and the Group*).

To date, the Group has raised approximately £32 million from a number of investors, including Inventages, one of the world's largest life-sciences, nutrition and wellness focused venture capital fund managers. On 31 December 2015, the Group had cash and cash equivalents of £983,654. In addition to the net proceeds of the Placing receivable by the Company, the Company will receive an additional £3.8 million upon Admission pursuant to the exercise of the W. Health Replacement Option referred to in paragraph 9.8 of Part 10 (*Additional Information*).

3 The Placing

The Placing comprises 21,666,662 New Shares which are to be issued by the Company. Of these:

(a) the Company intends to issue 20,226,665 New Shares pursuant to the Placing Agreement for an aggregate subscription price of approximately £30.3 million; and

(b) the Company intends to issue 1,439,997 New Shares pursuant to the Subscription Agreements for an aggregate subscription price of £2.2 million,

together representing appropriately 20 per cent. of the issued share capital of the Company immediately following Admission.

The Company will grant to each participant in the Placing 7 Warrants to subscribe for Ordinary Shares for every 13 Placing Shares subscribed, exercisable at a price of 150p per Ordinary Share.

The Company will bear one-off fees and expenses of approximately £2.4 million in connection with the Placing and Admission.

Under the Placing, Ordinary Shares and Warrants are being offered to certain existing shareholders, institutional and other investors in the United Kingdom and elsewhere outside the United States in reliance on Regulation S and in accordance with locally applicable laws and regulations.

All of the Placing Shares will be issued, at the Placing Price, which will be payable in full. The currency of the Placing is pounds sterling.

The distribution of this document and the placing of the Placing Shares and the Warrants are subject to the selling restrictions set out in paragraph 9 below.

When admitted to trading, the Ordinary Shares will be registered with ISIN number GB00BYV81293 and SEDOL number BYV8129 and trade under the symbol ''STX''. The rights attaching to the Ordinary Shares will be uniform in all respects and they will form a single class for all purposes.

When admitted to trading, the Warrants will be registered with ISIN GB00BD97Z526 and SEDOL number BD97Z52 and trade under the symbol ''STXW''.

Immediately following Admission, it is expected that not less than 22.5 per cent. of the Company's issued share capital will be held in public hands.

Completion of the Placing will be subject to, *inter alia*, the satisfaction of conditions contained in the Placing Agreement, including Admission occurring and the Placing Agreement not having been terminated in accordance with its terms. The Placing cannot be terminated once Admission has taken place. Further details of the Placing Agreement are set out in paragraph 5 below and in paragraphs 13.1 and 13.2 of Part 10 (*Additional Information*).

4 Placing Arrangements

The Company, the Directors and Liberum have entered into the Placing Agreement pursuant to which, on the terms and subject to certain conditions contained in the Placing Agreement which are customary in agreements of this nature, Liberum has agreed to use its reasonable endeavours to procure subscribers for 20,226,665 Placing Shares pursuant to the Institutional Placing.

In addition, certain existing Shareholders and other investors have agreed to subscribe for 1,439,997 New Shares at the Placing Price pursuant to the Subscription Agreements with the Company.

The Placing Agreement provides that the obligations of Liberum are conditional upon, *inter alia*, Admission becoming effective by 8.00 a.m. on 26 February 2016 (or such later date and time as the Company may agree with Liberum (being not later than 11 March 2016)) and the Subscription Agreements and the Reorganisation Agreements having been entered into and becoming and continuing to be enforceable against each of the parties thereto (subject only to Admission).

The Placing Agreement provides for Liberum to be paid commission by the Company in respect of the Placing upon Admission. Any commissions received by Liberum may be retained, and any Placing Shares acquired by them may be retained or dealt in, by them for their own benefit.

Further details of the terms of the Placing Agreement and the Subscription Agreements are set out in paragraph 13 of Part 10 (*Additional Information*).

5 Reasons for the Placing and use of proceeds

The Company intends to use its existing cash balances (including the proceeds of the W. Health Replacement Option) and the net proceeds from the Placing of £30.1 million with the clear primary objective of commercialising and further developing its lead product, Feraccru. In light of this, the net proceeds from the Placing are intended to be applied to the following workstreams:

(a) Commercial development

  (i) to prepare for and launch Feraccru into the European markets using its own dedicated central and field based commercial team initially targeted on IDA in IBD; and

  (ii) to fund expansion of the Group's central infrastructure to support the growth of its business;

(b) Clinical development

  (i) to continue to develop Feraccru through conducting further clinical trials to support its commercial plans and to allow further regulatory approvals in other indications and markets including the US;

  (ii) to fund regulatory and chemistry, manufacturing and control costs in relation to the launch of Feraccru; and

  (iii) to fund limited further development of PTL's assets.

In addition to the net proceeds from the Placing, revenues generated from Feraccru will be used to help fund further business development, particularly to expand the approval and commercial uptake of Feraccru and for the further development of the Company's assets including R&D to continue to drive expansion of Feraccru geographically and by medical indication. In addition, in the event all of the Warrants are exercised, the Directors expect to receive gross proceeds of approximately £17.5 million of additional funds that, with the monies referred to above, will be used to finance the Company's business plan set out in Part 2 (*Information on the Company and the Group*) of this document. The Company may also raise additional finance through up-front payments from the out licensing of its development pipeline, and also through securing debt financing facilities on appropriate terms.

The Directors believe that the Placing and Admission will raise the Company's profile and enhance its ability to launch and market Feraccru. By raising awareness within the market generally, and with potential marketing and out-licence partners, the Company is expected to be able to attract and retain high quality employees to assist in its development.

6 Lock-up Arrangements

Each of Carl Sterritt, Richard Jones, Andrew Heath, Christian Schweiger, W. Health and IRORPH have entered into lock-up arrangements pursuant to which they have agreed to be subject to a twelve month lock-up period, during which time, subject to certain exceptions, they may not issue, offer, sell or contract to sell, or otherwise dispose of any Ordinary Shares, Warrants or any Ordinary Shares that may be issued pursuant to the exercise of Warrants, or enter into any transaction with the same economic effect as the foregoing (each a ''Disposal''). In addition, they have also agreed that any Disposal in the subsequent six-month period will be undertaken by Liberum (for so long as Liberum remains the Company's nominated adviser and broker) from time to time.

Further details of these arrangements, which are contained in the Lock-up Agreements, are set out in paragraph 9.12 of Part 10 (*Additional Information*).

7 Dealing Arrangements

It is expected that Admission will take place at 8.00 a.m. on 26 February 2016. It is expected that Ordinary Shares and Warrants allocated to investors will be delivered in Uncertificated Form and settlement will take place through CREST on Admission.

Each investor will be required to undertake to pay the Placing Price for the Ordinary Shares sold to such investor in such manner as shall be directed by Liberum.

8 CREST

CREST is a paperless settlement system enabling securities to be transferred from one person's CREST account to another's without the need to use share certificates or written instruments of transfer. With effect from Admission, the Articles will permit the holding of Ordinary Shares and Warrants under the CREST system.

Application has been made for the Ordinary Shares and Warrants to be admitted to CREST with effect from Admission. Accordingly, settlement of transactions in the Ordinary Shares and Warrants following Admission may take place within the CREST system if any Shareholder so wishes. CREST is a voluntary system and, after Admission, holders of Ordinary Shares and Warrants who wish to receive and retain share certificates will be able to do so.

9 Selling Restrictions

The distribution of this document and the offering of Placing Shares and Warrants in certain jurisdictions may be restricted by law and therefore persons into whose possession this document comes should inform themselves about and observe any such restrictions. Any failure to comply with these restrictions may constitute a violation of the securities laws of any such jurisdiction.

No action has been or will be taken in any jurisdiction that would permit a public offering of the Placing Shares or Warrants, or possession or distribution of this document or any other offering material in any country or jurisdiction where action for that purpose is required. Accordingly, the Placing Shares and Warrants may not be offered or sold, directly or indirectly, and neither this document nor any other offering material or advertisement in connection with the Placing Shares and Warrants may be distributed or published in or from any country or jurisdiction, except in circumstances that will result in compliance with all applicable rules and regulations of any such country or jurisdiction. Persons into whose possession this document comes should inform themselves about and observe any restrictions on the distribution of this document and the offer of Placing Shares contained in this document. Any failure to comply with these restrictions may constitute a violation of the securities laws of any such jurisdiction. This document does not constitute an offer to subscribe for or purchase any of the Placing Shares or Warrants to any person in any jurisdiction to whom it is unlawful to make such offer or solicitation in such jurisdiction.

10 Directors, Senior Management, Employees and Key Advisors

10.1 Directors

The current members of the Board and their principal functions, together with a brief description of their business experience and principal business activities outside the Group, are set out below:

Name	Position	Date of birth
Dr Andrew Heath	Non-Executive Chairman	30 April 1948
Carl Sterritt	Chief Executive Office and co-founder	16 October 1968
Richard CM Jones	Chief Financial Officer and Company Secretary	27 May 1966
James Karis	Non-Executive Director	1 May 1948
Peter Llewellyn-Davies	Non-Executive Director	13 April 1958

The business address of each director is: Northern Design Centre, Baltic Business Quarter, Gateshead Quays NE8 3DF.

Dr Andrew Heath. Dr Andrew Heath is a highly experienced healthcare and biopharmaceutical executive with in-depth knowledge of US and UK capital markets and international experience in marketing, sales, R&D and business development. Dr Heath is currently Deputy Chairman and Senior Independent Director of Oxford BioMedica plc and is a non-executive director of Novacyt SA and Integrated Healing Technologies, LLC. He was formerly a director of the BioIndustry Association and he was Chief Executive Officer of Protherics plc from 1999 to 2008, taking the company from 30 to 350 staff and managing its eventual acquisition by BTG plc for £220 million. Prior to this Andrew served as Vice President of Marketing and Sales, for Astra Inc. in the US and held senior positions at Glaxo, Sweden.

Carl Sterritt. With around 20 years' of management and executive level experience in pharmaceutical development and commercialisation in both large and small company settings, Carl has led the Group as its CEO since he co-founded the SHG Group in 2008 and PTL in 2011. Previously, Carl held senior management roles at United Therapeutics and Encysive Pharmaceuticals, working on innovative therapies for the treatment of pulmonary arterial hypertension. Carl joined United Therapeutics to establish the company's European operations in preparation for the marketing approval of Remodulin, running the subsidiary for six years. In collaboration with physicians in Germany, he was responsible for and holds patents related to United Therapeutics' decision to develop and commercialise treprostinil; now successfully commercialised in the US as Tyvaso. Carl was instrumental in the successful commercial launch of Thelin and the rapid growth of Encysive's European operations. Carl founded the SHG Group after Encysive was acquired by Pfizer Inc. for more than $300m.

Richard CM Jones ACA. Richard was appointed a Non-Executive Director of SHG in early 2010 and Chief Financial Officer in April 2011. Richard has advised the Group since its inception in his previous role as an investment banker with both Brewin Dolphin Securities and Investec Bank. Richard has a strong track record in advising clients on a wide range of transactions and fundraisings including IPOs, M&A and fundraisings. With more than 10 years' advisory experience in the investment banking industry, his particular focus was in the healthcare sector where he developed extensive experience with a broad range of clients including private companies, private equity and UK and European quoted companies. Richard qualified as a Chartered Accountant with Coopers & Lybrand in 1991.

James Karis. James is a life sciences and healthcare industry executive with over 35 years of experience in the pharmaceutical, healthcare services, technology and medical device industries. A proven entrepreneur he is also an experienced board member for public and private companies with extensive experience in corporate strategy, M&A and all aspects of company financing. He is currently, Chief Executive Officer of privately held Mapi Group, a company focused on conducting late phase studies as well as providing regulatory and reimbursement support to the pharmaceutical and device Industries. James has previously held senior management and executive roles at CollabRx, Entelos, Inc., PAREXEL International, Pharmaco International and Baxter International. He has a B.S. in Management and Economics from Purdue University and a M.A. in Applied Economics from The American University.

Peter Llewellyn-Davies. Peter is a strategic CFO with an over 25 year track record in international M&A deals, company turnarounds, licensing transactions and financing activities with particular experience in chemical and healthcare industries. Peter has been CFO of Medigene AG since 2012 and has supported the turnaround process by outlicensing marketed and legacy products and enhancing shareholder value with a large international investor base. Prior to that he was CFO of Wilex AG, having orchestrated their IPO in 2006 to fund a later stage pipeline and conclude subsequent partnering deals and acquisitions. Peter is a founder of Accellerate Partners, focused on executing change and supporting private and listed companies and advising venture capital and private equity firms. Peter read business management, banking, marketing and controlling in London, St. Gallen and Munich, and has a certificate in business studies from the University of London. Peter was nominated for appointment to the Board pursuant to the Relationship Agreement.

10.2 Senior Management

In addition to the Executive Directors, the current senior managers with responsibility for day-to-day management of the Group's business are set out below.

David Childs (Manufacturing Director). David joined the SHG Group in August 2011 as Director of Manufacturing. During his tenure at Wellcome, GlaxoWellcome and GlaxoSmithKline (GSK), David gained over 18 years' experience in chemical and pharmaceutical development. He has led several successful projects including Promacta and Relovair and has successfully led teams of scientists in the development of synthetic processes and analytical methodologies. During his tenure at GSK, David worked closely with several outsourcing partners as well as across GSK's international network of manufacturing sites to ensure timely product delivery and successful methodology transfer between internal and external sites.

Angela Hildreth (Group Financial Controller and Head of Human Resources). Angela has been the SHG Group Financial Controller since 2011. She was instrumental in setting up, managing and running all financial processes across three countries including group consolidations and multi-currency cash and treasury management. In addition, as Head of Human Resources, she has been directly responsible for all aspects of building and developing a highly skilled team of around 20 people. She manages financial aspects of the Group's operations and is directly involved in commercial contractual negotiations as well as influencing the Group's strategy as part of the senior leadership team.

Kate Hopkinson (Marketing Director). Kate has over 14 years of sale and marketing experience within the pharmaceutical industry, having worked for Lundbeck, Abbott Laboratories and Vifor Pharma. Whilst at Vifor, Kate led marketing and operational planning for Ferinject, an iron IV therapy which saw double digit growth in the UK and Ireland. She joined the Company in October 2015 in order to work on the launch and commercialisation of Feraccru in Europe.

Dr Jackie Mitchell (VP Regulatory Affairs). Jackie has over 20 years' experience in regulatory affairs. She holds an MA in biochemistry from Lady Margaret Hall at Oxford University, where she also obtained a doctorate in immunology and molecular biology. Following completion of her academic studies, Jackie spent a number of years working as a research scientist, including a period at Johns Hopkins School of Medicine in Baltimore, USA. Since moving into the pharmaceutical industry, Jackie has worked in regulatory affairs for large, medium and small pharmaceutical companies, including Boehringer Ingelheim, Abbott and Archimedes. She has been involved in a broad range of global, EU and national applications across many therapeutic areas and has led several major regulatory projects, including successful MAA and NDA submissions for NCEs, including Kaletra and Humira. Jackie has run SHG's regulatory activities since 2012.

Karen Nugent (VP Clinical Development). Karen has 20 years of experience of strategic and operational leadership of clinical development portfolios within both blue chip companies such as Pfizer and fast growing pharmaceutical businesses such as Napp and most recently Biogen-Idec. Karen possesses comprehensive experience and demonstrates a successful track record in the design, budgeting and execution of all the facets of full phase programmes used to support successful product development and commercialisation; whilst building and developing highly motivated teams.

Dr Mark Sampson (VP Medical Affairs). Mark has more than 25 years of medical practice and pharmaceutical development and commercialisation experience. He has outstanding pedigree in the development and leadership of Medical Affairs at companies such as GSK, Amgen and Gilead, having been a key element of a number of successful commercialisation projects. Mark is a highly experienced pharmaceutical physician who combines broad medical knowledge and business acumen, with an outstanding record of achievement in Medical Affairs at affiliate, regional and global levels across pharmaceutical, biotech and consumer products. In addition Mark was a member of the UK Prescription Medicines Code of Practice Appeals Board for 13 years.

Paul Steckler *(VP Commercial Operations)*. Paul Steckler is a commercial leader with more than 17 years of pharmaceutical experience across a broad range of therapeutic areas. Paul gained a BSc in Microbiology & Virology from Warwick University before joining the pharmaceutical industry in 1997. Paul spent the majority of his career at Pfizer working across multiple therapy areas including Genotropin, Somavert, Zyvoz, Vfend, Ecalta, Rapamune and Tygacil. Since leaving Pfizer in 2012 Paul has worked with a number of smaller pharmaceutical companies with a focus on speciality medications including launching Jinarc (in polycystic kidney disease) for Otsuka Pharmaceuticals.

10.3 Employees

As at 31 December 2015, the Group employed sixteen people and retained five contractors. Five are in commercial operations, five are in clinical operations, two in Supply Chain, one in Quality, one in regulatory and seven in management, finance and administration.

10.4 Key Advisors

The Group has access to a range of experts and opinion leaders who have been involved in the development of Feraccru or PT20 and/or the related clinical and non-clinical trials. These include:

- **Dr Tariq Ahmad, MRCP, D.Phil, MB ChB** – Dr Ahmad leads the Exeter Inflammatory Bowel Disease service and was co-author of the ''Guidelines for the management of IBD in adults'', on behalf of the IBD Section of the British Society of Gastroenterology (''BSG''). Dr Ahmad is a medical advisor to the national patient group, Crohn's and Colitis UK and the current medical editor of the patient newsletter. Dr Ahmad is a member of the BSG IBD clinical studies group and was an investigator in the Phase 3 Study for Feraccru.

- **Dr Gert Van Assche, MD, PhD** – Dr Gert Van Assche is Associate Professor of Medicine, Department of Internal Medicine, University of Leaven, Belgium. He is Vice President of the Flemish Gastroenterology Association and member of the Editorial Board of Gut, Journal of Crohn's and Colitis and Alimentary Pharmacology and Therapeutics and former Chair of the Educational Committee of the European Crohn's and Colitis Association (''ECCO''). Dr Van Assche chaired the symposia on Feraccru hosted by SHG at ECCO in Barcelona in February 2015 and will chair the UEGW symposium in October 2015.

- **Dr Geoffrey A Block, MD, CCRI** – Dr. Block is the Director of Clinical Research at Denver Nephrology. He serves as an advisor and consultant for several pharmaceutical and biotechnology companies interested in developing medicine to help patients with kidney disease. Dr Block has been working with PT20 since 2012 as a consultant and he was the principal investigator in the Phase 2B pivotal study in PT20 that completed in 2015.

- **Dr Bernd Bokemeyer, MD** – Dr Bokemeyer was the principal investigator in the pivotal Phase 3 Study for Feraccru and was the single biggest recruiter of patients to the study. He was co-author on the peer reviewed publication on Feraccru in February 2015 and continues to act as a consultant to SHG on further clinical development in respect of Feraccru.

- **Professor Christoph Gasche, MD** – Professor Gasche led and co-authored the publication of the outcome of the Phase 3 Study in Feraccru, having been chief investigator in Austria for the Phase 3 Study. Professor Gasche was co-author of the 2007 ECCO Guidelines and the 2015 ECCO Guidelines. He was a speaker at the UEGW symposium in October 2015.

- **Dr Tariq Iqbal, MB, BCH, BA, MD, FRCP** – Dr Tariq Iqbal is based at the Queen Elizabeth Hospital, Birmingham. His primary research interest is in iron metabolism and he is an expert on the pathogenesis and management of anaemia. Dr Iqbal is a member of the National Gastroenterology Comprehensive Clinical Research Network. Dr Iqbal is on the steering committee of the European Crohn's and Colitis Organisation (''ECCO'') and was co-author of the 2015 European Consensus on the Diagnosis and Management of Iron Deficiency and Anaemia in IBD (''2015 ECCO Guidelines''). Dr Iqbal presented at ECCO 2015 and he presented at the UEGW symposium in October 2015.

- **Professor Jonathan Powell** – Professor Powell is Head of Bio-Mineral Research at the MRC's Human Nutrition Research (''HNR'') Elsie Widdowson Laboratory in Cambridge. Within HNR, his work focuses on (i) the absorption of iron and diagnosis and treatment of iron deficiency; (ii) the role of minerals, in inflammatory and anti-inflammatory processes of the gastrointestinal tract and (iii) the development of novel mineral-based therapeutics. Dr Powell and his team were the inventors of the patented technology behind PT20 and have advised PTL since PTL acquired the licence from the MRC in late 2011.

- **Professor Andreas Stallmach** – Professor Andreas Stallmach is Head of the Department of Gastroenterology, Hepatology and Infectious Diseases, University Hospital of Jena, Germany. Professor Stallmach has run a large number of studies particularly in Chrohn's and Colitis and was a principal investigator for Feraccru's pivotal Phase 3

Study in Germany. He has submitted a publication on Feraccru which is currently under review: Expert Opinion on Pharmacotherapy, ''Ferric maltol: A novel oral iron supplement for the treatment of IDA in IBD''.

- **Dr Michael Stockham, Ph.D** – Following the Group's acquisition of Feraccru from Vitra Pharmaceuticals, Dr Stockham has continued to advise the Group as a consultant and has actively assisted in the continued development of the intellectual property relating to Feraccru, including the filing of new patents related to Feraccru.

11 Relationship Agreement with W. Health

Upon Admission, it is expected that W. Health will hold approximately 49.99 per cent. of the voting rights attached to the issued share capital of the Company.

On 12 February 2016, the Company and W. Health entered into the Relationship Agreement, which will, conditional upon Admission, regulate the on going relationship between the Company and W. Health. The principal purpose of the Relationship Agreement is to ensure:

- that the Company is able to comply with the AIM Rules and will be carrying on an independent business as its main activity;
- that all transactions and arrangements between the Group and W. Health and their respective associates are at arm's length and on normal commercial terms;
- that W. Health and its associates will not take any action that would have the effect of preventing the Company from complying with its obligations under the AIM Rules, or propose or procure the proposal of a shareholder resolution which is intended or appears to be intended to circumvent the proper application of the AIM Rules or the Disclosure and Transparency Rules;
- that (save with the prior written consent of the Company) W. Health will not take any action and shall procure that none of its associates nor any other person acting in concert with W. Health shall take any action which would cause its holding, when combined with any shareholding of its associates or any other person acting in concert with W. Health, to reach or exceed 50 per cent. of the voting rights of the Company; and
- that the Board will manage the Company in the interests of the Shareholders as a whole.

The Relationship Agreement will continue for so long as (a) the Ordinary Shares remain admitted to trading on AIM and (b) W. Health holds at least 10 per cent. of the Company's issued share capital.

Under the Relationship Agreement, W. Health is able to nominate one Director for appointment to the Board for so long as it holds over 20 per cent. of the Company's issued share capital. As it is expected immediately following Admission that W. Health will hold more than 20 per cent. of the voting rights attached to the issued share capital of the Company, it will be entitled to nominate one non-executive Director for appointment to the Board. The first such nominee is Peter Llewellyn-Davies.

The Directors believe that the terms of the Relationship Agreement will enable the Company to comply with the AIM Rules and allow the Group to carry on its business independently of W. Health.

Conflicts of interest

Immediately following Admission, it is expected that W. Health will hold approximately 49.99 per cent. of the voting rights attached to the issued share capital of the Company.

Save as set out in the paragraph above, there are no potential conflicts of interest between any duties owed by the Directors or Senior Management to the Company and their private interests or other duties.

12 Corporate Governance

12.1 QCA Code/Corporate Governance Code

The Board recognises the importance of sound corporate governance and with that aim, the Company has adopted policies and procedures which reflect to principles of the QCA's Corporate Governance Guidelines for Smaller Quoted Companies ("**QCA Code**") as are appropriate to a company whose shares are admitted to trading on AIM. The Company has chosen to comply with the Corporate Governance Code in so far as it is appropriate for a company whose shares are admitted to trading on AIM.

12.2 Board composition and independence

The Board is committed to the highest standards of corporate governance and maintaining a sound framework for the control and management of the Group's business. The Board is responsible for leading and controlling the Group and has overall authority for the management and conduct of the Group's business and the Group's strategy and development. The Board is also responsible for ensuring the maintenance of a sound system of internal control and risk management (including financial, operational and compliance controls, and for reviewing the overall effectiveness of systems in place) and for the approval of any changes to the capital, corporate and/or management structure of the Group.

On Admission, the Board will comprise of five members, being the Chairman, two executive directors and two non-executive directors.

12.3 Audit, Remuneration and Nomination Committees

The Board has established Audit, Remuneration and Nomination Committees with effect from Admission.

12.3.1 Audit Committee

The Audit Committee has responsibility for, among other things, the monitoring of the financial integrity of the financial statements of the Group and the involvement of the Group's auditors in that process, reviewing the effectiveness of the Group's internal control systems and risk management systems and overseeing the process for managing risks across the Group, including reviewing the Group's corporate risk profile. It focuses in particular on compliance with legal requirements, accounting standards and ensuring that an effective system of internal financial controls is maintained. The ultimate responsibility for reviewing and approving the annual report and accounts and the half-yearly reports remains with the Board. The Audit Committee will normally meet at least two times a year at the appropriate times in the reporting and audit cycle.

The terms of reference of the Audit Committee cover such issues as membership and the frequency of meetings, together with quorum requirements and the right to attend meetings. The responsibilities of the Audit Committee covered in the terms of reference are: external audit, internal audit, financial reporting, internal controls and risk management. The terms of reference also set out the authority of the committee to carry out its responsibilities.

The members of the Audit Committee are Peter Llewellyn-Davies and James Karis. Peter Llewellyn-Davies is regarded as having recent and relevant financial experience. The committee chair is Peter Llewellyn-Davies.

12.3.2 Remuneration Committee

The Remuneration Committee has responsibility for determination of specific remuneration packages for each of the executive directors and any applicable senior executive management of the Company, including pension rights and any compensation payments and recommending and monitoring the level and structure of remuneration for senior management, and the implementation of share option, or other performance-related schemes. The Remuneration Committee will meet at least once a year.

The terms of reference of the Remuneration Committee cover such issues as membership and the frequency of meetings, together with the quorum requirements and the right to attend meetings. The responsibilities of the Remuneration Committee covered in the terms of reference are: determining and monitoring policy on and setting levels of remuneration, contracts of employment, early termination, performance-related pay, pension arrangements,

reporting and disclosure, share-schemes and remuneration consultants. The terms of reference also set out the reporting responsibilities and the authority of the committee to carry out its responsibilities.

The members of the Remuneration Committee are James Karis and Peter Llewellyn-Davies. The committee is chaired by James Karis.

12.3.3 Nomination Committee

The Nomination Committee is responsible for considering and making recommendations to the Board in respect of appointments to the Board, the Board committees and the chairmanship of the Board committees. It is also responsible for keeping the structure, size and composition of the Board under regular review, and for making recommendations to the Board with regard to any changes necessary. The Nomination Committee will meet at least once a year.

The Nomination Committee's terms of reference deal with such things as membership, quorum and reporting responsibilities. It also considers succession planning, taking into account the skills and expertise that will be needed on the Board in the future.

The members of the Nomination Committee are Dr Andrew Heath, Peter Llewellyn-Davies and James Karis. The committee is chaired by Dr Andrew Heath.

12.4 Share Dealing Code

The Directors are required to comply with Rule 21 of the AIM Rules for Companies relating to Directors' and applicable employees' dealings in the Company's securities and to this end the Company has adopted an appropriate share dealing code. The share dealing code provides *inter alia* all employees require the consent of Richard Jones, the Company's Chief Financial Officer before trading in any securities of the Company. The Company will be responsible for taking all reasonable steps to ensure compliance by the Directors and applicable employees with the share dealing code and the Aim Rules for Companies.

13 Takeover Regulation

The City Code is issued and administered by The Panel on Takeovers and Mergers. The Company is subject to the City Code and therefore its Shareholders are entitled to the protections afforded by the City Code.

Under Rule 9 of the City Code when (i) a person acquires an interest in shares which (taken together with shares he and persons acting in concert with him are interested) carry 30 per cent or more of the voting rights of a company subject to the City Code, or (ii) any person who, together with persons acting in concert with him, is interested in shares which in the aggregate carry not less than 30 per cent. of the voting rights of a company, but does not hold shares carrying more than 50 per cent. of the voting rights of the company subject to the City Code, and such person, or any persons acting in concert with him, acquires an interest in any other shares which increases the percentage of the shares carrying voting rights in which he is interested, then, in either case, that person, together with the person acting in concert with him, is normally required to extend offers in cash, at the highest price paid by him (or any persons acting in concert with him) for shares in the company within the preceding 12 months, to the holders of any class of equity share capital whether voting or non-voting and also to the holders of any other class of transferable securities carrying voting rights. However this obligation may be waived with the consent of the Panel where the acquisition which triggers an obligation for a mandatory offer under Rule 9 of the City Code is an acquisition of New Shares and the company has obtained the approval of over 50 per cent. of its independent shareholders in advance of such increase.

On Admission, W. Health will hold 54,062,901 Ordinary Shares representing approximately 49.99 per cent. of the issued share capital of the Company. Save as disclosed in the paragraph below, as the Ordinary Shares which W. Health will be interested in carry 30 per cent. or more of the voting rights in the Company and W. Health would not hold shares carrying more than 50 per cent. of the voting rights in the Company, W. Health may not increase its percentage shareholding in the Company without being subject to the provisions of Rule 9 of the City Code.

In addition, pursuant to the terms of the Warrant Instrument, W. Health has the right (subject to certain limits) to subscribe for one Ordinary Share for each Warrant its holds in consideration for the payment of the Placing Price in cash from the date of the Warrant Instrument up until (and including) 30 June 2017. Further details of the Warrant Instrument are set out in Part 9 (*Particulars of the Warrants*) of this document.

Upon Admission, W. Health will hold 1,945,640 Warrants. If W. Health were to exercise its rights in relation to all of the Warrants, and assuming that none of the other Warrants in issue are exercised, W. Health's shareholding in the Company would increase to approximately 50.9 per cent.

The Panel has confirmed to the Company, on an ex parte basis, that it would not require W. Health to make a mandatory offer under Rule 9 of the City Code as a result of it increasing the percentage of Ordinary Shares in which it is interested in if its interest in the issued share capital of the Company has increased as a result only of the issue of New Shares following the exercise of the Warrants. This confirmation has been given by the Panel on the basis that the consequences of the exercise of the Warrants have been fully disclosed to prospective investors in this Admission Document. Accordingly, if W. Health increased its shareholding in the Company to over 50 per cent. through the exercise of some or all of its Warrants, it would then be free to further increase its holding of Ordinary Shares without any obligation to make a mandatory offer under Rule 9 of the City Code.

Notwithstanding the above, pursuant to the terms of the Relationship Agreement between the Company and W. Health, W. Health has agreed (save with the prior written consent of the Company) not take any action, including exercising any rights to subscribe for Ordinary Shares attaching to a Warrant, which would cause its holding to reach or exceed 50 per cent. of the voting rights of the Company. Further details of the Relationship Agreement are set out in paragraph 11 above.

Under the Act, if a takeover offer (as defined in section 974 of the Act) is made for the Ordinary Shares and the offeror were to acquire, or unconditionally contract to acquire, not less than 90 per cent. in value of the shares to which the takeover offer relates (the "**Takeover Offer Shares**") and not less than 90 per cent. of the voting rights attached to the Takeover Offer Shares, within three months of the last day on which its offer can be accepted, it could acquire compulsorily the remaining 10 per cent. It would do so by sending a notice to outstanding shareholders telling them that it will acquire compulsorily their Takeover Offer Shares and then, six weeks later, it would execute a transfer of the outstanding Takeover Offer Shares in its favour and pay the consideration to the Company, which would hold the consideration on trust for outstanding shareholders. The consideration offered to the shareholders whose Takeover Offer Shares are acquired compulsorily under the Act, must, in general, be the same as the consideration that is available under the takeover offer.

The Act also gives minority shareholders a right to be bought out in certain circumstances by an offeror who has made a takeover offer. If a takeover offer related to all the Ordinary Shares and at any time before the end of the period within which the offer could be accepted the offeror held or had agreed to acquire not less than 90 per cent. of the shares to which the offer related, any holder of Ordinary Shares to which the offer related who had not accepted the offer could by a written communication to the offeror require it to acquire those Ordinary Shares. The offeror is required to give any shareholder notice of his rights to be bought out within one month of that right arising. The offeror may impose a time limit on the rights of the minority shareholders to be bought out, but that period cannot end less than three months after the end of the acceptance period. If a shareholder exercises his or her rights, the offeror is bound to acquire those Ordinary Shares on the terms of the offer or on such other terms as may be agreed.

14 Dividend Policy

The Directors intend, for the foreseeable future, to retain future earnings, if any, to finance the development of the Group's business and do not intend to pay any dividends. The Company may revise its dividend policy after considering *inter alia* the Group's financial resources and prospects, research, development and commercialisation expenditure, investment requirements and actual and forecast cashflows.

15 Terms and conditions of the Institutional Placing

MEMBERS OF THE PUBLIC ARE NOT ELIGIBLE TO TAKE PART IN THE INSTITUTIONAL PLACING. THESE TERMS AND CONDITIONS ARE FOR INFORMATION PURPOSES ONLY AND ARE DIRECTED ONLY AT: (A) PERSONS IN MEMBER STATES OF THE EUROPEAN ECONOMIC AREA WHO ARE QUALIFIED INVESTORS AS DEFINED IN SECTION 86(7) OF THE FSMA, AS AMENDED, ''QUALIFIED INVESTORS'') BEING PERSONS FALLING WITHIN THE MEANING OF ARTICLE 2(1)(E) OF THE PROSPECTUS DIRECTIVE INCLUDES ANY RELEVANT IMPLEMENTING DIRECTIVE MEASURE IN ANY MEMBER STATE; (B) IN THE UNITED KINGDOM, QUALIFIED INVESTORS WHO ARE PERSONS WHO: (I) FALL WITHIN ARTICLE 19(5) OF THE FINANCIAL SERVICES AND MARKETS ACT 2000 (FINANCIAL PROMOTION) ORDER 2005 (THE ''ORDER''); (II) FALL WITHIN ARTICLE 49(2)(A) TO (D) (HIGH NET WORTH COMPANIES, UNINCORPORATED ASSOCIATIONS, ETC) OF THE ORDER; OR (III) ARE PERSONS TO WHOM IT MAY OTHERWISE BE LAWFULLY COMMUNICATED (ALL SUCH PERSONS TOGETHER BEING REFERRED TO AS ''RELEVANT PERSONS''). THESE TERMS AND CONDITIONS MUST NOT BE ACTED ON OR RELIED ON BY PERSONS WHO ARE NOT RELEVANT PERSONS. ANY INVESTMENT OR INVESTMENT ACTIVITY TO WHICH THESE TERMS AND CONDITIONS RELATES IS AVAILABLE ONLY TO RELEVANT PERSONS AND WILL BE ENGAGED IN ONLY WITH RELEVANT PERSONS.

(a) Introduction

These terms and conditions apply to persons making an offer to acquire Placing Shares and Warrants under the Institutional Placing. Each person to whom these conditions apply, as described above, who confirms his agreement to Liberum and the Company (whether orally or in writing) to acquire Placing Shares and Warrants under the Institutional Placing (an ''**Investor**'') hereby agrees with Liberum and the Company to be bound by these terms and conditions as being the terms and conditions upon which Placing Shares and Warrants will be sold under the Institutional Placing. An Investor shall, without limitation, become so bound if Liberum confirms to such Investor: (i) the Placing Price; and (ii) its allocation of Placing Shares and Warrants under the Institutional Placing.

Upon being notified of the Placing Price and its allocation of Placing Shares and Warrants in the Institutional Placing, an Investor shall be contractually committed to acquire the number of Placing Shares and Warrants allocated to them at the Placing Price and, to the fullest extent permitted by law, will be deemed to have agreed not to exercise any rights to rescind or terminate or otherwise withdraw from such commitment. Dealing may not begin before any notification is made.

(b) Agreement to acquire Placing Shares and Warrants

Conditional on: (i) Admission occurring and becoming effective by 8.00 a.m. (London time) on 26 February 2016 (or such later time and/or date as the Company and Liberum may agree) and on the Placing Agreement being otherwise unconditional in all respects and not having been terminated in accordance with its terms on or before Admission; and (ii) the confirmation mentioned under paragraph (a) above, an Investor agrees to become a member of the Company and agrees to acquire Placing Shares and Warrants at the Placing Price. The number of Placing Shares and Warrants acquired by such Investor under the Institutional Placing shall be in accordance with the arrangements described above.

(c) Payment for Placing Shares and Warrants

Each Investor undertakes to pay the Placing Price for the Placing Shares and Warrants acquired by such Investor in such manner as shall be directed by Liberum. In the event of any failure by an Investor to pay as so directed by Liberum, the relevant Investor shall be deemed hereby to have appointed Liberum or its nominee to sell (in one or more transactions) any or all of the Placing Shares and Warrants in respect of which payment shall not have been made as so directed and to have agreed to indemnify on demand Liberum in respect of any liability for stamp duty and/or stamp duty reserve tax arising in respect of any such sale or sales.

(d) Representations and warranties

By receiving this document, each Investor and, to the extent applicable, any person confirming his agreement to acquire Placing Shares and Warrants on behalf of an Investor or authorising Liberum to notify an Investor's name to the Registrar, is deemed to acknowledge, agree, undertake, represent and warrant to each of Liberum, the Registrar and the Company that:

(i) the Investor has read this document in its entirety and acknowledges that its participation in the Institutional Placing shall be made solely on the terms and subject to the conditions set out in these terms and conditions, the Placing Agreement and the Articles. Such Investor agrees that these terms and conditions and the contract note issued by Liberum to such Investor represent the whole and only agreement between the Investor, Liberum and the Company in relation to the Investor's participation in the Institutional Placing and supersedes any previous agreement between any of such parties in relation to such participation. Accordingly, all other terms, conditions, representations, warranties and other statements which would otherwise be implied (by law or otherwise) shall not form part of these terms and conditions. Such Investor agrees that none of the Company, Liberum nor any of their respective officers or directors will have any liability for any such other information or representation and irrevocably and unconditionally waives any rights it may have in respect of any such other information or representation;

(ii) the content of this Admission Document is exclusively the responsibility of the Company and the Directors and that neither Liberum nor any person affiliated with Liberum or acting on its behalf is responsible for or shall have any liability for any information, representation or statement contained in this Admission Document or any supplementary admission document (as the case may be) or any information previously published by or on behalf of the Company or any member of the Group and will not be liable for any decision by an Investor to participate in the Institutional Placing based on any information, representation or statement contained in this Admission Document or otherwise;

(iii) the Investor has not relied on Liberum or any person affiliated with Liberum in connection with any investigation of the accuracy of any information contained in this document or their investment decision;

(iv) in agreeing to acquire Placing Shares and Warrants under the Institutional Placing, the Investor is relying on this Admission Document or any supplementary admission document (as the case may be) and not on any draft thereof or other information or representation concerning the Group, the Institutional Placing or the Placing Shares and Warrants. Such Investor agrees that neither the Company nor Liberum nor their respective officers, directors or employees will have any liability for any such other information or representation and irrevocably and unconditionally waives any rights it may have in respect of any such other information or representation;

(v) Liberum is not making any recommendations to Investors or advising any of them regarding the suitability or merits of any transaction they may enter into in connection with the Institutional Placing, and each Investor acknowledges that participation in the Institutional Placing is on the basis that it is not and will not be a client of Liberum and that Liberum is acting for the Company and no one else, and Liberum will not be responsible to anyone else for the protections afforded to its clients, and that Liberum will not be responsible for anyone other than the Company for providing advice in relation to the Institutional Placing, the contents of this Admission Document or any transaction, arrangements or other matters referred to herein, and Liberum will not be responsible for anyone other than the relevant party to the Placing Agreement in respect of any representations, warranties, undertakings or indemnities contained in the Placing Agreement or for the exercise or performance of Liberum's rights and obligations thereunder, including any right to waive or vary any condition or exercise any termination right contained therein;

(vi) save in the event of fraud on its part (and to the extent permitted by the rules of the FCA), neither Liberum nor any of its directors or employees shall be liable to an Investor for any matter arising out of the roles of Liberum as the Company's nominated adviser

and broker or otherwise, and that where any such liability nevertheless arises as a matter of law each Investor will immediately waive any claim against Liberum and any of its respective directors and employees which an Investor may have in respect thereof;

(vii) if the laws of any place outside the United Kingdom are applicable to the Investor's agreement to acquire Placing Shares and Warrants in the Institutional Placing, such Investor has complied with all applicable laws and such Investor will not infringe any applicable law as a result of such Investor's agreement to acquire Placing Shares and Warrants under the Institutional Placing and/or acceptance thereof or any actions arising from such Investor's rights and obligations under the Investor's agreement to acquire Placing Shares and Warrants under the Placing and/or acceptance thereof or under the Articles;

(viii) all actions, conditions and things required to be taken, fulfilled and done (including the obtaining of necessary consents) in order: (i) to enable the Investor lawfully to enter into, and exercise its rights and perform and comply with its obligations to acquire the Placing Shares and Warrants under the Institutional Placing; and (ii) to ensure that those obligations are legally binding and enforceable, have been taken, fulfilled and done. The Investor's entry into, exercise of its rights and/or performance under, or compliance with its obligations under the Institutional Placing, does not and will not violate: (a) its constitutive documents; or (b) any agreement to which the Investor is a party or which is binding on the Investor or its assets;

(ix) it understands that no action has been or will be taken in any jurisdiction by the Company, Liberum or any other person that would permit a public offering of the Placing Shares and Warrants, or possession or distribution of this document, in any country or jurisdiction where action for that purpose is required; and that, if the Investor is in a relevant member state, it is: (i) a legal entity which is authorised or regulated to operate in the financial markets or, if not so authorised or regulated, its corporate purpose is solely to invest in securities; (ii) a legal entity which has two or more of: (a) an average of at least 250 employees during the last financial year; (b) a total balance sheet of more than €43,000,000; and (c) an annual net turnover of more than €50,000,000, in each case as shown in its last annual or consolidated accounts; (iii) otherwise permitted by law to be offered and sold Placing Shares and Warrants in circumstances which do not require the publication by the Company of a prospectus pursuant to Article 3 of the Prospectus Directive or other applicable laws; or (iv) in the case of any Placing Shares and Warrants acquired by an Investor as a financial intermediary, as that term is used in Article 3(2) of the Prospectus Directive, either:

(1) the Placing Shares and Warrants acquired by it in the Institutional Placing have not been acquired on behalf of, nor have they been acquired with a view to their placing or resale to, persons in any relevant member state other than qualified investors, as that term is defined in the Prospectus Rules, or in circumstances in which the prior consent of Liberum has been given to the placing or resale; or

(2) where Placing Shares and Warrants have been acquired by it on behalf of persons in any relevant member state other than qualified investors, the placing of those Placing Shares and Warrants to it is not treated under the Prospectus Rules as having been made to such persons;

(x) to the fullest extent permitted by law, the Investor acknowledges and agrees to the disclaimers contained in this document and acknowledges and agrees to comply with the selling restrictions set out in this document;

(xi) the Placing Shares and Warrants have not been and will not be registered under the Securities Act or under the securities legislation of, or with any securities regulatory authority of, any state or other jurisdiction of the United States or under the applicable securities laws of Australia, Canada, Japan, the Republic of Ireland or the Republic of South Africa or where to do so may contravene local securities laws or regulations;

(xii) the Investor is, and at the time the Placing Shares and Warrants are acquired, will be located outside the United States and eligible to participate in an ''offshore transaction'' as defined in and in accordance with Regulation S;

(xiii) the Investor is not acquiring the Placing Shares and Warrants as a result of any "directed selling efforts" as defined in Regulation S or as a result of any form of general solicitation or general advertising (within the meaning of Rule 502(c) of Regulation D under the Securities Act);

(xiv) if it is acquiring the Placing Shares and Warrants for the account of one or more other persons, it has full power and authority to make the representations, warranties, agreements and acknowledgements herein on behalf of each such account;

(xv) the Investor is acquiring the Placing Shares and Warrants for investment purposes only and not with a view to any resale, distribution or other disposition of the Placing Shares in violation of the Securities Act or any other United States federal or applicable state securities laws;

(xvi) the Company is not obliged to file any registration statement in respect of resales of the Placing Shares and Warrants in the United States with the US Securities and Exchange Commission or with any state securities administrator;

(xvii) the Company, and any registrar or transfer agent or other agent of the Company, will not be required to accept the registration of transfer of any Placing Shares and Warrants acquired by the Investor, except upon presentation of evidence satisfactory to the Company that the foregoing restrictions on transfer have been complied with;

(xviii) the Investor invests in or purchases securities similar to the Placing Shares and Warrants in the normal course of its business and it has such knowledge and experience in financial and business matters as to be capable of evaluating the merits and risks of an investment in the Placing Shares and Warrants;

(xix) the Investor has conducted its own investigation with respect to the Company and the Placing Shares and Warrants and has had access to such financial and other information concerning the Company and the Placing Shares and Warrants as the Investor deemed necessary to evaluate the merits and risks of an investment in the Placing Shares and Warrants, and the Investor has concluded that an investment in the Placing Shares and Warrants is suitable for it or, where the Investor is not acting as principal, for any beneficial owner of the Placing Shares and Warrants, based upon each such person's investment objectives and financial requirements;

(xx) the Investor or, where the Investor is not acting as principal, any beneficial owner of the Placing Shares and Warrants, is able to bear the economic risk of an investment in the Placing Shares and Warrants for an indefinite period and the loss of its entire investment in the Placing Shares and Warrants;

(xxi) there may be adverse consequences to the Investor under tax laws in other jurisdictions resulting from an investment in the Placing Shares and Warrants and the Investor has made such investigation and has consulted such tax and other advisors with respect thereto as it deems necessary or appropriate;

(xxii) the Investor is not a resident of the United States, Australia, Canada, Japan, the Republic of Ireland or the Republic of South Africa and acknowledges that the Placing Shares and Warrants have not been and will not be registered nor will a prospectus be prepared in respect of the Placing Shares and Warrants under the securities legislation of the United States, Australia, Canada, Japan, the Republic of Ireland or the Republic of South Africa and, subject to certain exceptions, the Placing Shares and Warrants may not be offered or sold, directly or indirectly, in or into those jurisdictions;

(xxiii) the Investor is liable for any capital duty, stamp duty and all other stamp, issue, securities, transfer, registration, documentary or other duties or taxes (including any interest, fines or penalties relating thereto) payable outside the UK by it or any other person on the acquisition by it of any Placing Shares and Warrants or the agreement by it to acquire any Placing Shares and Warrants;

(xxiv) in the case of a person who confirms to Liberum on behalf of an Investor an agreement to acquire Placing Shares and Warrants under the Institutional Placing and/or who authorises Liberum to notify such Investor's name to the Registrar, that person represents and warrants that he has authority to do so on behalf of the Investor;

(xxv) the Investor has complied with its obligations in connection with money laundering and terrorist financing under the Proceeds of Crime Act 2002, the Terrorism Act 2000 and the Money Laundering Regulations 2007 and any other applicable law concerning the prevention of money laundering and, if it is making payment on behalf of a third party, that satisfactory evidence has been obtained and recorded by it to verify the identity of the third party as required by the Money Laundering Regulations 2007 and, in each case, agrees that pending satisfaction of such obligations, definitive certificates (or allocation under the CREST system) in respect of the Placing Shares and Warrants comprising the Investor's allocation may be retained at Liberum's discretion;

(xxvi) the Investor agrees that, due to anti-money laundering and the countering of terrorist financing requirements, Liberum and/or the Company may require proof of identity of the Investor and related parties and verification of the source of the payment before the application can be processed and that, in the event of delay or failure by the Investor to produce any information required for verification purposes, Liberum and/or the Company may refuse to accept the application and the moneys relating thereto. It holds harmless and will indemnify Liberum and/or the Company against any liability, loss or cost ensuing due to the failure to process this application, if such information as has been required has not been provided by it or has not been provided on a timely basis;

(xxvii) the Investor is not, and is not applying as nominee or agent for, a person which is, or may be, mentioned in any of sections 67, 70, 93 and 96 of the Finance Act 1986 (depository receipts and clearance services);

(xxviii) the Investor has complied with and will comply with all applicable provisions of FSMA with respect to anything done by the Investor in relation to the Institutional Placing in, from or otherwise involving the UK;

(xxix) if the Investor is in the UK, the Investor is a person: (i) who has professional experience in matters relating to investments falling within article 19(5) of the Order; or (ii) a high net worth entity falling within article 49(2)(a) to (d) of the Order; or (iii) are persons to whom it may otherwise be lawfully communicated, and in all cases is capable of being categorised as a Professional Client or Eligible Counterparty for the purposes of the FCA Conduct of Business Rules;

(xxx) if the Investor is in the EEA, the person is a "Professional Client/Eligible Counterparty" within the meaning of Annex II/Article 24 (2) of MiFID and is not participating in the Institutional Placing on behalf of persons in the EEA other than professional clients or persons in the UK and other Member States (where equivalent legislation exists) for whom the Investor has authority to make decisions on a wholly discretionary basis;

(xxxi) each Investor in a relevant member state of the EEA who acquires any Placing Shares and Warrants under the Institutional Placing contemplated hereby will be deemed to have represented, warranted and agreed with each of Liberum and the Company that: (i) it is a qualified investor within the meaning of the law in that relevant member state implementing Article 2(1) of the Prospectus Directive; and (ii) in the case of any Placing Shares and Warrants acquired by it as a financial intermediary, as that term is used in Article 3(2) of the Prospectus Directive: (A) the Placing Shares and Warrants acquired by it in the Institutional Placing have not been acquired on behalf of, nor have they been acquired with a view to their offer or resale to, persons in any relevant member state other than qualified investors, as that term is defined in the Prospectus Directive, or in other circumstances falling within Article 3(2) of the Prospectus Directive and the prior consent of Liberum has been given to the offer or resale; or (B) where Placing Shares and Warrants have been acquired by it on behalf of persons in any relevant member state other than qualified investors, the offer of those Placing Shares and Warrants to it is not treated under the Prospectus Directive as having been made to such persons;

(xxxii) in the case of a person who confirms to Liberum on behalf of an Investor an agreement to acquire Placing Shares and Warrants under the Institutional Placing and who is acting on behalf of a third party, that the terms on which the Investor (or any person acting on its behalf) are engaged enable it to make investment decisions in relation to securities on that third party's behalf without reference to that third party;

(xxxiii) the exercise by Liberum of any rights or discretions under the Placing Agreement shall be within its absolute discretion and Liberum need not have any reference to any Investor and shall have no liability to any Investor whatsoever in connection with any decision to exercise or not to exercise or to waive any such right and each Investor agrees that it shall have no rights against Liberum or any of its directors or employees under the Placing Agreement;

(xxxiv) it irrevocably appoints any director of Liberum as its agent for the purposes of executing and delivering to the Company and/or its registrars any documents on its behalf necessary to enable it to be registered as the holder of any of the Placing Shares and Warrants agreed to be taken up by it under the Institutional Placing and otherwise to do all acts, matters and things as may be necessary for, or incidental to, its acquisition of any Placing Shares and Warrants in the event of its failure so to do;

(xxxv) it will indemnify and hold the Company, Liberum and its respective affiliates harmless from any and all costs, claims, liabilities and expenses (including legal fees and expenses) arising out of or in connection with any breach of the representations, warranties, acknowledgements, agreements and undertakings in this paragraph 15 and further agrees that the provisions of this paragraph 15 will survive after completion of the Institutional Placing;

(xxxvi) Liberum may, in accordance with applicable legal and regulatory provisions, engage in transactions in relation to the Placing Shares and Warrants and/or related instruments for its own account and, except as required by applicable law or regulation, Liberum will not make any public disclosure in relation to such transactions; and

(xxxvii) Liberum and each of its respective affiliates, each acting as an investor for its or their own account(s), may bid or subscribe for and/or purchase Placing Shares and Warrants and, in that capacity, may retain, purchase, offer to sell or otherwise deal for its or their own account(s) in the Placing Shares and Warrants, any other securities of the Company or other related investments in connection with the Institutional Placing or otherwise. Accordingly, references in this document to the Placing Shares and Warrants being offered, subscribed, acquired or otherwise dealt with should be read as including any offer to, or subscription, acquisition or dealing by Liberum and/or any of its respective affiliates, acting as an investor for its or their own account(s). Neither Liberum nor the Company intend to disclose the extent of any such investment or transaction otherwise than in accordance with any legal or regulatory obligation to do so.

The Company and Liberum will rely upon the truth and accuracy of each of the foregoing representations, warranties and undertakings.

(e) Supply and disclosure of information

If any of Liberum, the Registrar or the Company or any of their respective agents request any information about an Investor's agreement to acquire Placing Shares and Warrants, such Investor must promptly disclose it to them and ensure that such information is complete and accurate in all respects.

(f) Miscellaneous

The rights and remedies of Liberum, the Registrar and the Company under these terms and conditions are in addition to any rights and remedies which would otherwise be available to each of them, and the exercise or partial exercise of one will not prevent the exercise of others.

(i) On application, each Investor may be asked to disclose, in writing or orally to Liberum:

(1) if he is an individual, his nationality; or

(2) if he is a discretionary fund manager, the jurisdiction in which the funds are managed or owned.

(ii) All documents will be sent at the Investor's risk. They may be sent by post to such Investor at an address notified to Liberum.

(iii) Each Investor agrees to be bound by the Articles (as amended from time to time) once the Placing Shares and Warrants which such Investor has agreed to acquire have been acquired by such Investor.

(iv) The provisions of this paragraph 15 may be waived, varied or modified as regards specific Investors or on a general basis by Liberum.

(v) The contract to acquire Placing Shares and Warrants and the appointments and authorities mentioned herein will be governed by, and construed in accordance with, the laws of England and Wales. For the exclusive benefit of Liberum, the Company and the Registrar, each Investor irrevocably submits to the exclusive jurisdiction of the English courts in respect of these matters. This does not prevent an action being taken against an Investor in any other jurisdiction.

(vi) In the case of a joint agreement to acquire Placing Shares and Warrants, references to an ''Investor'' in these terms and conditions are to each of such Investors and such joint Investors' liability is joint and several.

(vii) Liberum and the Company each expressly reserve the right to modify the Institutional Placing (including, without limitation, its timetable and settlement) at any time before allocations of Placing Shares and Warrants under the Institutional Placing are determined.

(viii) The Institutional Placing is subject to the satisfaction of the conditions contained in the Placing Agreement and the Placing Agreement not having been terminated. Further details of the terms of the Placing Agreement are contained in paragraph 13 of Part 10 (*Additional Information*) of this document.

16 Further information

Prospective investors should read the whole of this document which provides additional information on the Company and not rely on summaries or individual parts only. In particular, the attention of prospective investors in drawn to Part 3 (*Risk Factors*) of this document, which contains a summary of the risk factors relating to any investment in the Ordinary Shares and Warrants.

PART 2

INFORMATION ON THE COMPANY AND THE GROUP

1 Overview

Shield Therapeutics is a specialty pharmaceutical company focused on the development and commercialisation of secondary care-focused prescription pharmaceuticals.

The Company's key products are Feraccru and PT20, two late-stage pharmaceuticals for the treatment of iron deficiency anaemia and systemic phosphate accumulation (otherwise known as hyperphosphatemia), respectively. In addition the Group has earlier stage assets that it intends to develop or out-licence over time.

1.1 Feraccru

Feraccru is a novel and effective oral ferric iron-based pharmaceutical product that the CHMP has given a unanimous positive opinion should be granted a marketing authorisation in all member states of the European Union. This marketing authorisation is scheduled to be issued in the first quarter of 2016. Initially Feraccru will be licensed to treat iron deficiency anaemia ("IDA") in patients with inflammatory bowel disease ("IBD"). A phased roll-out of commercialisation of Feraccru is expected to commence within the EU during 2016 targeted to treat IBD patients who have failed treatment on Oral Ferrous Products or for whom such treatment is unsuitable. The Directors believe Feraccru has an achievable global peak annual sales opportunity in excess of £500 million.

After some early scientific work on the technology at St Thomas' Hospital, London in the late 1990's, the Feraccru technology was developed by a small independent pharmaceutical company, Vitra Pharmaceuticals. Following this research, Vitra Pharmaceuticals filed a number of patents, particularly in respect to manufacturing methods. The Group acquired Feraccru from Vitra Pharmaceuticals in 2010.

The Directors believe there is a large and attractive market of patients with IDA whose only current option is either no therapy or intravenous iron therapy, as currently available oral treatments demonstrate limited effectiveness due to negative adverse event profiles leading to low levels of compliance. Intravenous therapies also have limitations as they are expensive to administer, require time consuming and inconvenient intermittent administration, and due to their potential to cause hypersensitivity reactions are required to be administered in a healthcare facility where resuscitation facilities are available.

To date, clinical studies conducted of Feraccru in IDA patients who have failed treatment on OFPs have demonstrated the potential for it to be an effective daily oral treatment in such patients providing an alternative therapy to intravenous iron.

The Company received a positive CHMP recommendation for Feraccru on 17 December 2015 and marketing authorisation is scheduled to be received from the European Commission in the first quarter of 2016. The Company expects to launch Feraccru in Europe following receipt of the marketing authorisation, with the UK being the launch country.

1.2 PT20

PT20 is a novel iron-based phosphate binder being developed for the treatment of hyperphosphatemia related to chronic kidney disease ("CKD") and has completed Phase 2 clinical trials.

PT20 was invented in the UK by leading Cambridge-based scientists and is exclusively licensed from the MRC. Patients with late-stage renal disease suffer from hyperphosphatemia, which enhances the risk of vascular calcification, leading to increased morbidity and mortality. Low phosphate diets and regular dialysis sessions are by themselves unable to prevent gradual phosphate accumulation, therefore, oral phosphate binders are routinely used to reduce absorption of phosphate and thereby reduce blood phosphate levels.

The Directors believe there is a large and attractive market for PT20. Current treatments are often limited by at least one of the following problems: limited therapeutic dosing range, low specificity, high pill loading, gastrointestinal side effects, calcium loading or significant toxicity concerns.

To date, studies conducted by the Company have demonstrated the potential of PT20 to deliver an effective treatment of hyperphosphatemia related to dialysis dependent CKD.

Whilst the Company has commenced planning for the Phase 3 development of PT20 including manufacturing scale up activity, the Company's near to medium term focus is on evaluating outlicensing deals with suitable partner(s) to assist in the funding of the final stage of clinical development prior to launch. The Company has received a number of enquiries from potential partners although discussions are at an early stage. As the Group develops the Company may look to devote capital to the development of PT20 and other assets as an alternative to outlicensing.

2 History and Background

2.1 Shield Holdings AG (''SHG'')

The SHG Group was formed in 2008 with the incorporation of Iron Therapeutics (UK) Limited (''ITU''). Carl Sterritt (the Company's CEO) and Christian Schweiger were two of the founding shareholders and they remain significant shareholders.

ITU's initial activities related exclusively to fundraising and identifying potential acquisition opportunities. During this period the founding shareholders formed the view that Switzerland was an appropriate jurisdiction to develop pharmaceuticals within a favourable tax environment. As a result, Iron Therapeutics Holdings AG and, subsequently, SHG were incorporated as new holding companies of the SHG Group.

On 23 February 2010, with initial investment from the SHG founders, Carl Sterritt and Christian Schweiger, ITH purchased the intellectual property relevant to Feraccru from Vitra Pharmaceuticals and acquired other related intellectual property from Pfylori Limited, a company under common ownership with Vitra Pharmaceuticals.

The SHG Group spent the period following this acquisition developing its clinical, regulatory and manufacturing strategy and raising sufficient capital to commence activities. In mid-2011 its first clinical trials commenced on Feraccru with the first patient recruited in August 2011.

Following the acquisition of Feraccru from Vitra Pharmaceuticals, and following an initial private round of fundraising of approximately £1.0 million, various discussions on potential collaborations took place with well-established private investors with profound expertise in the pharma sector, including AOP Pharma. IRORPH, a new Austrian registered investment vehicle of the WAKS foundation was introduced by AOP Pharma as a stategic investor. AOP Pharma and IRORPH share the same management and are associates for the purposes of the AIM Rules for Companies. IRORPH committed £3.9 million in total. The first tranche of IRORPH's investment comprised a subscription of £1.1 million and was completed on 28 October 2010.

Further private funding rounds were completed in mid 2011 raising a total of approximately £1.1 million. In May 2011 an investment of £15.2 million in total was agreed with Inventages through its investment vehicle, W. Health LP. The first tranche of this investment comprised a subscription of £3.6 million which completed on 6 June 2011. Further tranches of this investment were received during 2012-2015 amounting to a further £11.6 million in total.

A further £1.5 million was invested in ITH in a new fundraising round in December 2014 from the WAKS foundation.

2.2 Phosphate Therapeutics Limited (''PTL'')

In 2011 negotiations commenced with the MRC to acquire worldwide licences in respect of certain patent rights and related know-how to develop and commercialise products for specific medical applications in the fields of phosphate binding for the treatment of renal diseases and/or intravenous iron for the treatment of iron deficiency anaemia.

As is common practice, the assets were agreed to be held in a separate investment vehicle. Accordingly, PTL was incorporated on 3 May 2011 as a private limited company in England and Wales by Carl Sterritt, Richard Jones, Laura Emery and Christian Schweiger.

The MRC Licence was entered into between PTL and the MRC on 22 December 2011 whereby the MRC granted PTL exclusive worldwide licences in respect of two patent families and related know-how to develop and commercialise products covered by the licensed

intellectual property in the fields of (i) phosphate binding for the treatment of renal diseases; and (ii) intravenous iron for the treatment of IDA. Further details are contained in paragraph 5.9 below and in paragraph 9.1 of Part 10 (*Additional Information*) of this document.

As part of the licence agreement, MRC took a minority equity interest in PTL. In addition, existing shareholders of SHG were given the opportunity to subscribe for shares in PTL.

At the same time, funding of £8.4m was secured from W. Health to establish operations and to progress the clinical, regulatory and manufacturing development of PT20, including the Phase 2b programme. The first tranche of this funding of £4.2m completed in February 2012 with further tranches of £3.2m and £1.1m received in July 2014 and March 2015 respectively.

A private fundraising round was agreed in July 2015 and completed in early September 2015 to raise an additional £0.9m of working capital for PTL.

2.3 Corporate Reorganisation

As well as sharing substantially similar shareholders, the Company's subsidiary, ITU, has supplied managerial and other support services to PTL under an operating agreement in relation to the management and product development activities of PTL's business. In addition, SHG and PTL are both developing products within the nephrology branch of medicine and the companies expect to have similar sales channels for their products. Accordingly, there was a clear commercial rationale for the Corporate Reorganisation to bring SHG and PTL together.

In preparation for Admission as part of the Corporate Reorganisation:

(a) W. Health has exercised the W. Health Replacement Option;

(b) IRORPH has exercised the IRORPH Top-up Option; and

(c) the Company has agreed to acquire the entire issued and to be issued share capital of PTL in consideration for the issue of 19,887,791 New Shares,

each of which are conditional upon, and will take effect upon, Admission. All other steps of the Corporate Reorganisation have completed.

Further details of the Corporate Reorganisation are contained in paragraph 2 of Part 10 (*Additional Information*).

The Corporate Reorganisation will result in the previous shareholders of SHG and PTL holding 77% and 23% respectively of the issued share capital of the Company, prior to the issue of Placing Shares pursuant to the Placing.

3 Key Strengths

3.1 Near term revenue potential

The Group filed its European application for marketing approval of Feraccru in December 2014. A positive CHMP recommendation for approval was received on 17th December 2015 and EU Commission ratification of the recommendation and hence marketing authorisation is scheduled to be received in the first quarter of 2016. The Group is planning to launch Feraccru in Europe in 2016 thus providing the potential for near term revenues.

3.2 Late stage assets that have either been approved or have delivered proof of concept

In addition to Feraccru's MAA already having received a positive opinion from the EU CHMP, the Phase 2b pivotal study with respect to PT20 has completed. For that reason, the Directors consider the Company to be a specialty pharmaceuticals company with multiple late stage assets.

3.3 Large market opportunities with unmet needs

Feraccru addresses a large and structurally growing market, with significant potential in the near term. GfK estimate there are approximately 1.4 to 1.5 million patients in Europe and the US with IBD who have the potential to be treated for IDA of which a significant proportion are currently ineffectively treated. GfK also estimate that there are over 3.4 million patients in the EU and US with IDA and CKD.

In the longer term, Feraccru has the opportunity to expand into a number of indications and geographies, thus significantly expanding the potential number of patients available for treatment.

In addition, during the life of the patent families relating to Feraccru, the Directors believe there is potential for Feraccru to be established in the primary care setting where there are a significant number of potential patients, particularly treatment of IDA in women's health and treatment of IDA in the elderly population. The Directors believe that Feraccru has an achievable global peak annual sales opportunity in excess of £500m.

The hyperphosphatemia market is large and growing and is driven by the rise in CKD in Western populations. GfK estimate there are over 650,000 patients in the EU and US on dialysis, the majority of whom are currently being treated with phosphate binders. Current therapies for the treatment of hyperphosphatemia are less than satisfactory and GfK's primary research indicated only a moderate degree of satisfaction with current phosphate binders.

3.4 Experienced Board and management team with extensive expertise

The Company has an experienced Board with extensive expertise in the pharmaceutical and biotechnology industry. Two of the Directors are members of the executive management team and, together with other highly experienced members of management, have been heavily involved in the development of the Group and key to driving its success to date. Carl Sterritt has been CEO since he co-founded the Group in 2008 and Richard Jones has been CFO since 2011.

The Board is supported by an experienced skilled management team which provides a strong platform for future growth and gives strategic direction to the development and commercialisation of the Group's products. Further details of the Directors and Senior Management are contained in paragraph 10 of Part 1 (*Key Information and Details of the Placing*) and in Part 10 (*Additional Information*).

In addition, during the development of its products, the Group has relied, and will continue to rely, on specialist commercial partners and suppliers including Contract Research Organisations and Contract Manufacturing Organisations.

3.5 Opportunity to create operational leverage across the product portfolio

Initially Feraccru and subsequently PT20, subject to any out-licensing, are intended to be sold using the Company's own commercial team with its own central and field-based commercial infrastructure in major markets in EU. The Company will target specialist prescribers based in hospitals and private clinics. This provides the potential for significant operational leverage which could be enhanced with selective small scale bolt-on acquisitions or in-licensing of allied products.

3.6 Strong intellectual property protection

The Group's assets are supported by a suite of strong intellectual property including key patents in major markets. With MAA and NDA approval, Feraccru will also benefit from data and marketing exclusivity in the EU (up to 10 years) and data exclusivity in the US (up to 3 years), respectively. The Group has been actively pursuing new patent applications and has filed 5 new patent applications for Feraccru since the acquisition from Vitra Pharmaceuticals in 2010. The new patents, if granted, will provide significant additional patent protection up to 2035 in relation to Feraccru.

For further details please refer to Part 7 (*Patent Agent's Report*) of this document.

3.7 Attractive financial profile

The proceeds of the Placing receivable by the Company and the future opportunity of receiving futher funds as a result of the exercise of the Warrants provides a strong financial platform for the growth of the Group. The Directors expect to generate near term revenues with inherently high gross margins following the planned launch of Feraccru in Europe in 2016. Whilst development activity will continue for the foreseeable future, the Directors believe that the level of R&D spend should be relatively modest compared to normal industry levels having regard to the potential revenues from Feraccru and PT20.

4 Feraccru

4.1 Overview

Feraccru is a novel and effective oral pharmaceutical product that, when approved, will initially be licensed in adults to treat Iron Deficiency Anaemia (''IDA'') in patients with inflammatory bowel disease (''IBD''). A phased roll-out of commercialisation of Feraccru is expected to commence within the EU during 2016 targeted to treat IBD patients who have failed treatment on Oral Ferrous Products or for whom such treatment is unsuitable. The Directors believe Feraccru has an achievable global peak annual sales opportunity in excess of £500m.

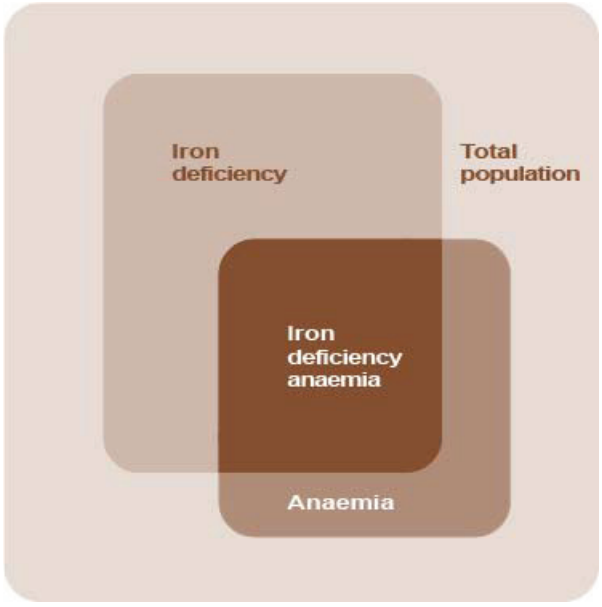
Feraccru consists of ferric iron chelated with maltol, a common food additive. Feraccru has been shown to be well tolerated in patients because any unabsorbed iron appears to be excreted in its bound state as Feraccru rather than being in its unbound state which irritates the gut.

Significant work on Feraccru, particularly in respect of the manufacturing methods, was undertaken by Dr Michael Stockham of Vitra Pharmaceuticals in the early 2000's. Dr Stockham overcame challenges in the production of ferric maltol and it was Dr Stockham who filed the core manufacturing patents which are further discussed in paragraph 4.5.5 below. In early 2010, the Group acquired Feraccru from Vitra Pharmaceuticals.

Background to Iron Deficiency and Iron Deficiency Anaemia

Iron Deficiency (''ID'') can range from a mild status with no apparent symptoms to the more serious condition of Iron Deficiency with anaemia. The WHO considers ID to be the most common and widespread nutritional disorder in the world. Iron status can be considered a continuum from iron deficiency with anaemia to iron deficiency with no anaemia to normal iron status.

Figure 1. Conceptual diagram of the relationship between Iron Deficiency and anaemia in a hypothetical population



Source: Iron deficiency anaemia: Assessment, prevention and control, World Health Organization, 2001.

Haemoglobin (found within red blood cells) is essential to life given its ability to carry oxygen from the lungs to all parts of the body. Iron is the key to the oxygen carrying capacity of haemoglobin. Red blood cells have a finite life cycle and are continually replaced. The iron from haemoglobin is recycled into new red blood cells. However, a small amount of iron is lost every day from the body and this is normally replaced by iron absorbed through the gut from the diet. If the amount of iron lost is greater than the amount absorbed from the gut then low iron levels within the body will result. A lack, or deficiency, of iron in the body will restrict the amount of oxygen that can be carried. The low amount of haemoglobin within red blood cells is known as anaemia.

According to the WHO, the levels of haemoglobin in the blood that define anaemia are less than 13 g/dL in adult men and less than 12 g/dL in adult women.[3,4,5] Levels defining anaemia in children and pregnant women are slightly different.

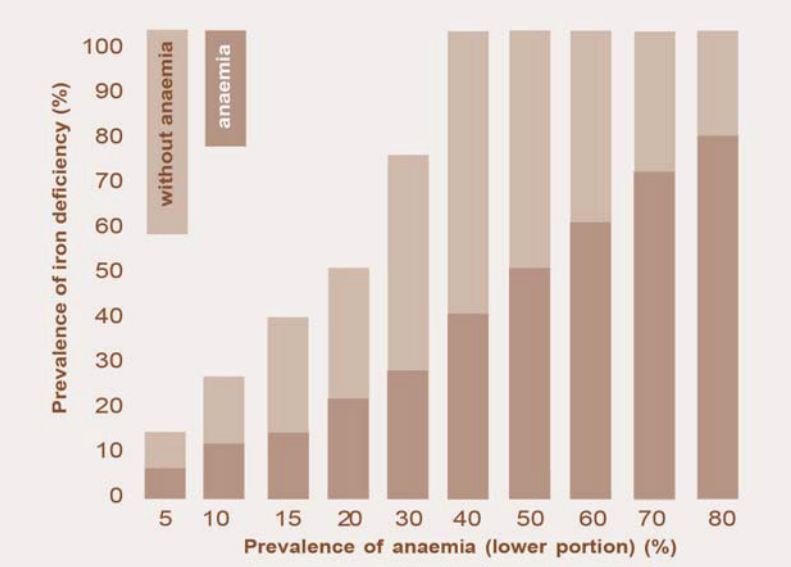
According to the WHO, the overall prevalence of anaemia in industrialised countries is 10.3% in women (rising to 22.7% in pregnant women), 4.3% in men, 12% in the elderly, 20.1% in young children and 5.9% in older children.[4] Prevalence rates are much higher in non-industrialised countries and, even in industrialised countries; most pregnant women are thought to suffer from some degree of iron deficiency.[5]

People with anaemia are restricted in how much oxygen can be transported from their lungs. Excess loss of iron (usually through some form of bleeding and loss of red blood cells), or reduced iron absorption (though low iron in the diet or diseases affecting the gut and its ability to absorb iron) will lead to iron deficiency, and eventually iron deficiency anaemia.

Anaemia is a leading cause of death related to childbirth and mortality in infants. Anaemia causes increased rates of infection and delays growth and educational development in children, and in turn has a large impact on productivity within developing countries. On an individual patient level anaemia causes reduced exercise tolerance, leading to fatigue and shortness of breath. Other symptoms include headaches and more frequent infection.

According to the WHO, the most significant contributor to the onset of anaemia globally is iron deficiency so that IDA and anaemia are often used synonymously, and the prevalence of anaemia has often been used as a proxy for IDA.[6,7] It is generally assumed that at least 50% of the cases of anaemia are due to iron deficiency.[7]

Figure 2. Projected prevalence of ID based on prevalence of IDA



Source: Iron deficiency anaemia: Assessment, prevention and control, World Health Organization, 2001.

Whilst children, menstruating and pregnant women are most likely to suffer from IDA, it is also a significant consequence, and symptom, of a number of diseases involving inflammation, loss of blood or the reduction in ability to absorb iron and is a leading cause of morbidity and mortality in many such indications. The most significant indications include:

- **Inflammatory Bowel Disease (''IBD'')** – IBD encompasses Ulcerative Colitis and Crohn's Disease. Up to 70% of patients with IBD have been shown to have anaemia and almost every IBD patient with anaemia shows some degree of iron deficiency.[8]

3,4,5 Iron deficiency anaemia: Assessment, prevention and control, World Health Organization, 2001.

6,7 B. Benoist, E. McLean, I. Egli, and M. Cogswell, Worldwide Prevalence of Anaemia 1993-2005: WHO Global Database on Anaemia, WHO, Geneva, Switzerland, 2008.

8 Wilson A, Reyes E, Ofman J. Prevalence and outcomes of anaemia in inflamatory bowel disease: a systemic review of the literature, Am J Med 2004; Avni T, Bieber A, Steinmetz T, Leibovici L, Gafter-Gvili A. Treatment of Anemia in Inflammatory Bowel Disease – Systematic Review and Meta-Analysis, 2013, DOI: 10.1371/journal.pone.0075540.

- **Chronic Kidney Disease (''CKD'')** – Anaemia is commonly associated with CKD. Studies have shown up to 60% of patients with CKD have IDA with the prevalence of IDA increasing with the severity of the underlying disease.[9]
- **Chronic Heart Failure (''CHF'')** – Iron Deficiency is a significant problem in CHF with up to 50% of CHF patients developing anaemia and being iron deficient with a significant impact on quality of life and functional status.[10]
- **Oncology** – Iron deficiency is a frequent complication of cancer and related cancer therapy such as chemotherapy with IDA having been reported in over 40% of chemotherapy patients.[11]

In addition to being a significant co-morbidity in several diseases, IDA is also a significant problem where it is associated with blood loss or lack of nutritional absorption of iron, including:

- **Women's Health** – As mentioned above, anaemia is a significant problem in women. In addition to pregnancy related anaemia, several other gynaecological complications such as Heavy Uterine Bleeding (''HUB'') and Fibroids contribute to IDA in otherwise healthy women.
- **Elderly** – Anaemia is a common problem in the elderly with incidence increasing with age. Studies have shown that approximately 10% of men and women over 65 years of age are anaemic, rising to approximately 20% in the over 85 age group.[12] Approximately 20% of this is related to iron deficiency or iron deficiency mixed with B12 and folate deficiency.[13]
- **Blood loss during surgery** – Loss of blood during major surgery commonly leads to IDA and frequently results in patients having to undergo iron supplementation with intravenous iron and blood transfusions; particularly in patients with poor pre-operative reserves of Hb and iron (e.g. patients with GI cancers or the elderly).
- **Bariatric Surgery** – This interventional surgery leads to the inability to absorb nutritional iron which, if untreated, leads to IDA. In the US over 220,000 procedures are carried out each year.[14]

Paediatric Anaemia

IDA is a significant problem in paediatric populations in both industrialised and non-industrialised countries. The highest prevalence of IDA in children is likely to occur approximately between 6 months to 3 years of age when iron stores can become depleted, the intake of breast or formula milk is decreasing and the solid food introduced often fails to provide sufficient iron.

Iron deficiency is also a common problem throughout childhood. Acceleration of growth in adolescence, particularly during the years of sexual maturation, also imposes increased requirements for iron. ID and IDA in children impacts on growth, maturation and educational development.

4.2 Current treatment options

The current treatment options for IDA can be summarised as being:

- **Diet** – A poor diet can be a contributory cause of IDA and therefore patients are typically advised to ensure adequate levels of iron-rich foods. In developing countries this, together with the use of iron cooking materials, can be an effective strategy to reduce anaemia in normal populations. However, improved diet only has limited impact in IDA.

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9 Fishbane S, Pollack S, Feldman H, Joffe M Iron indices in chronic kidney disease in the National Health and Nutritional Examination Survey 1988-2004, Clin J Am Soc Nephrol 2009.

10 Ebner N., von Haehling S. Iron deficiency in heart failure: A practical guide. Nutrients. 2013;5:3730-3739. doi: 10.3390/nu5093730.

11 M. Aapro, A. Österborg, P. Gascón, H. Ludwig, Y. Beguin. Prevalence and management of cancer-related anaemia, iron deficiency and the specific role of i.v. iron, Annals of Oncology, 2012, 1954-1962, DOI: 10.1093/annonc/mds112.

12 Patel K.V. Epidemiology of anemia in older adults. Semin Hematol. 2008;45(4):210-217.

13 Patel K.V. Epidemiology of anemia in older adults. Semin Hematol. 2008;45(4):210-217.

14 Growth Industry https://www.diabetes.org.uk/upload/Professional%20members%20area/Diabetes%20Upate/Winter%202010/Growthindustry_new.pdf Accessed September 2010.

- **Treatment using Oral Ferrous Products** – Typically, OFPs are a first line therapy for the treatment of IDA. OFPs are routinely prescribed in general practice and are seemingly attractive because of their low purchase price. However, OFPs have a high level of non-compliance of up to 50% due to poor tolerability.[15]

- **Treatment using intravenous iron (''IV'') products** – In general, IV iron is a second line therapy typically prescribed by specialists. Guidelines have been issued by ECCO and other such organisations for the treatment of IDA in patients with IBD and CKD, recommending the administration of IV iron. This recommendation is built on the recognition that OFPs are often poorly tolerated resulting in lack of compliance and therefore result in poor haemoglobic (''Hb'') correction.[16] However, as previously noted, IV therapies have limitations as they are expensive, intermittent, have the potential to cause hypersensitivity reactions and are inconvenient.

- **Blood Transfusion** – In severe cases of IDA, a blood transfusion may be given to replace the lost red-blood cells. However, this is typically seen as a last resort. Blood transfusions do not of themselves correct low iron stores and concomitant iron replacement therapy is usually needed.

- **Surgical intervention to prevent blood loss** – This treatment option may be appropriate for a very small proportion of patients with IDA to treat certain conditions causing significant blood loss such as bleeding from the gut, or menorrhagia (heavy menstrual bleeding).

Oral Ferrous Products and Ferrous Intolerance

Gastrointestinal (''GI'') adverse reactions are common with oral administration of ferrous iron. OFPs are recommended to be taken with food, to lessen some of the GI side effects. This means that oral ferrous iron has to be given in large doses because of interactions between ferrous iron and food leading to formation of insoluble complexes. However the large doses and substantial amount of unabsorbed iron in the gut result in significant adverse GI reactions such as constipation, abdominal pain, dyspepsia, stool discoloration, and nausea/vomiting. Studies have shown that between 30% and 80% of IBD patients typically report adverse events with OFPs.[17]

The problems noted in respect of using OFPs are particularly acute in IBD.[18] The ferrous iron is oxidised in the stomach releasing free radicals which are potentially damaging to the already inflamed gut wall and may produce a range of gastrointestinal symptoms and discomfort.

Further, there is an additional difficulty treating patients with high pH levels in the gut, particularly due to other medications taken (such as proton-pump inhibitors) as it exacerbates precipitation and results in poor absorption.

There have been many attempts to improve upon ferrous iron formulations without significant improvement in the efficacy/safety ratio.

Intravenous Iron (''IV iron'')

In both the EU and US markets IV iron products are typically indicated for patients with IDA who are intolerant of or unresponsive to OFPs.

However, intravenous iron medicines have a small, but significant, risk of causing allergic, hypersensitivity reactions which can be life threatening. In 2013, based on recommendations by the Committee for Medicinal Products for Human Use (''CHMP''), the European Medicines Agency (''EMA'') reiterated the requirement for IV iron to be administered in a healthcare

15 Lindgren S, Wikman O, Befrits R, Blom H, Eriksson A, Granno C, et al. Intravenous iron sucrose is superior to oral iron sulphate for correcting anaemia and restoring iron stores in IBD patients: a randomized, controlled, evaluator-blind, multicentre study. Scand J Gastroenterol 2009:1-8.

16 Tolkien Z, Stecher L, Mander AP, Pereira DI, Powell JJ. Ferrous sulphate supplementation causes significant gastrointestinal side-effects in adults: a systematic review and meta-analysis. PLoS One. 2015 Feb 20;10(2).

17 Tolkien Z, Stecher L, Mander AP, Pereira DI, Powell JJ. Ferrous sulphate supplementation causes significant gastrointestinal side-effects in adults: a systematic review and meta-analysis. PLoS One. 2015 Feb 20;10(2).

18 Lindgren S, Wikman O, Befrits R, Blom H, Eriksson A, Granno C, et al. Intravenous iron sucrose is superior to oral iron sulphate for correcting anaemia and restoring iron stores in IBD patients: a randomized, controlled, evaluator-blind, multicentre study. Scand J Gastroenterol 2009:1-8.

facility where resuscitation facilities are available.[19] Furthermore, allergic reactions are unpredictable and caution is warranted with every dose of IV iron even if previous administrations have been well tolerated. In addition, there are increased costs associated with the administration of IV iron.

IV iron cannot in practice be used as a maintenance therapy in patients who have ongoing iron loss or poor oral intake. Regular monitoring of Hb and iron status is necessary to know when to repeat IV iron infusions and the irregular nature of administration often leads to patients becoming anaemic between treatments. Further, there can be significant inconvenience for some patients in scheduling and attending a hospital visit.

Oral delivery of iron in the ferric form

Iron can be delivered in the ferrous form or ferric form. OFPs are delivered orally in the ferrous form and IV Iron is typically delivered in the ferric form. Iron can also be delivered orally in the ferric form.

Studies have shown that ferric iron preparations have fewer gastro-intestinal adverse reactions than ferrous preparations as ferric iron is already oxidised and so damaging radicals are not released as there is no oxidisation process.[20]

Prior to Feraccru, the problem that existed in delivering ferric iron orally is that it forms insoluble complexes resulting in poor bioavailability.

4.3 Feraccru's technology

Feraccru consists of ferric iron chelated with maltol and is taken as an oral product for the treatment of IDA.

Feraccru overcomes the limitations of current treatment options in the following ways:

- Feraccru does not require hospital-based administration;
- Unlike other ferric products, Feraccru remains in a soluble state when passing through the GI tract. This means that much lower doses can be given to treat IDA;
- As Feraccru does not have to be given with food and can be taken on an empty stomach; this means much lower doses can be given to treat IDA compared to OFP's; and
- The smaller amount of iron in the gut means that the risk of adverse reactions is reduced in subjects sensitive to OFPs.

In essence, the technology behind Feraccru is a way of delivering ferric iron to the body through oral administration without the problems of bioavailability and poor absorption evident in other oral iron products. This route of administration allows the body's own regulation system to absorb as much iron as is required depending on the level of IDA. The technology around the design of the ferric maltol complex itself ensures that the ferric iron is protected until it gets to the place in the body where it is utilised and does not form insoluble polymers which would otherwise cause the ferric iron to become insoluble and therefore unavailable for absorption.

The ferric iron is protected by virtue of the molecular structure of Feraccru, a diagram of which is shown below. The ferric iron (shown in red) can barely be seen as it is surrounded by the large maltol ligands (shown in blue). This structure means the iron is shielded from the gut by the bulky maltol molecules.

19 EMA CHMP Article 31 2013. New Recommendations to manage risk of Allergic Reactions with IV-iron containing medicines. EMMA 1579491/2013.

20 Gasche C et al. 2014. Correcting Iron Deficiency Anaemia in IBD: A Pivotal Phase 3 Study of a Novel Oral Ferric Iron; Gasche C et al. 2014. Inflammatory Bowel disease.

Figure 3. Structure of Feraccru compound

Source: Company

Feraccru is not, of itself, absorbed into the bloodstream as an entity. The ferric iron and maltol separate at the point of absorption. The iron is then available to the body and the maltol is metabolised and ultimately excreted in the urine. Any Feraccru that is not absorbed passes through the GI tract intact and is excreted. Maltol is an FDA Generally Recognised As Safe ("GRAS") substance and is widely used as a flavouring agent or a pharmaceutical excipient.

Feraccru has been shown to be well tolerated and able to therefore effectively treat IDA in subjects with IBD. In studies, subjects who failed treatment on OFPs (and therefore would be typically treated with IV iron) responded positively to Feraccru and tolerated treatment over the 64 week period.

4.4 Market opportunity

The Directors believe that:

- there is a large and attractive market for Feraccru initially as a treatment for IDA in patients with IBD, and particularly for those who have failed treatment on OFPs (or for whom such treatment is unsuitable) and whose only current treatment option is intravenous iron therapy or no therapy at all.
- IBD patients are considered the hardest IDA population to treat with existing oral therapies due to their high inherent intolerance to OFPs and therefore the higher dependence on more complex and expensive IV products.
- the compelling efficacy and safety data available on Feraccru in patients with IBD via the Phase 3 Study will establish Feraccru in patients with IBD at a relatively similar price to the drug only cost of IV iron. In the medium term there are a number of indications treated by secondary care physicians where IDA is a significant co-morbidity.
- by expanding Feraccru's label from the IBD population, Feraccru can become well established as the therapy of choice for patients who failed treatment on OFPs or for whom it is unsuitable, ahead of IV Iron.
- in the longer term, given the high prevalence of IDA, for example in the elderly, in the female population generally and specifically in women of child-bearing age, the Directors see significant potential for Feraccru as an effective iron deficiency treatment which can be administered to patients by general practice / primary care physicians.

The current market for iron products is large and growing. Galenica Limited in their 2014 report published in March 2015 estimated the global market to be approximately £1.6 billion per annum as at December 2014.[21] This market is delineated by Galenica into two segments:

- approximately £1.0 billion represented by existing Oral Ferrous Products; and
- approximately £0.6 billion represented by IV and other parenteral iron products.[22]

21 Galenica Limited Annual Report 2014.
22 Galenica Limited Annual Report 2014.

GfK estimate there are approximately 1.4 to 1.5 million patients in Europe and the US with IBD who have the potential to be treated for IDA of which a significant proportion are currently ineffectively treated. GfK also estimate that there are over 3.4 million patients in the EU and US with IDA and CKD. Given the significant level of ferrous intolerance, the large estimated number of patients receiving ineffective treatment and the rising penetration of IV iron the Directors believe the market potential is significant.

In the core markets of the EU and US in the two primary indications of IBD and CKD, the Directors believe Feraccru has an achievable global peak annual sales opportunity in excess of £500 million.

Market entry strategy for Feraccru

The Group's strategy in relation to the market entry of Feraccru is as follows:

- **Feraccru will be targeted at patients who have failed treatment on OFPs** – This is an important aspect of the commercial approach. Commercially, Feraccru is not targeting or seeking to be compared with the wide range of mostly generic and low priced OFPs in the market. By having an initially narrow label focused on the hard to treat IBD population and having conducted its Phase III study in patients that had previously failed treatment with OFPs, Feraccru will be commercially focused on patients who are either currently on IV therapy, or are otherwise currently treated ineffectively with OFPs or are unwilling to take them.
- **Feraccru is initially targeted at patients with IDA in IBD** – The Group's pivotal Phase 3 Study was conducted in IBD patients both because all of the historical clinical data for Feraccru was in IBD but, also because the IBD population is well recognised as being prone to failure on OFPs due to the patients' underlying conditions. Therefore, the positive results of the pivotal Phase 3 Study, which had a drop-out rate of less than 5% over twelve months, indicated very good efficacy and tolerability of Feraccru in this difficult to treat population. If the Group successfully develops this indication in difficult to treat patients, the Directors believe it will be easier to gain wide acceptance of Feraccru as standard of care in a number of other indications where IDA is an issue.
- **Initial focus on Europe** – The Group's management team has significant experience in launching products into the European market. The current MAA is for a centralised approval covering the EU as well as the European Economic Area countries (Norway, Iceland and Liechtenstein).
- **Commercialisation in-house** – A key aspect of the Group's approach will be to develop and maintain its own commercial team including a suitable field-based sales and marketing team in the key markets in Europe. This will allow the Company to retain full economic rights to Feraccru. As Feraccru is initially targeting a specific indication (IBD) with specialist GI consultants, typically hospital or private clinic based, the number of prescribing physicians is relatively low and can be covered by a relatively small field-based team. Other European countries will be serviced via experienced marketing partners where establishing a direct field team would not be cost effective. One key distribution agreement is already in place covering Austria and certain central European countries and Middle-East for Feraccru (see below in this paragraph 4.4 for further information).
- **Commercialisation in the US** – The Company plans either to establish its own commercial team in the US or to pursue an out-licence strategy for the US market dependant upon the likely timing of approval of Feraccru in the US. The Directors currently anticipate this in 2019. This strategy will be informed by the experience in Europe. Certain out-licence discussions have commenced but are at an early stage. In the US, the Company intends to utilise the clinical data from both the pivotal Phase 3 Study in IBD and the planned study in CKD to seek a wider initial label. In the longer term, the Company plans to conduct further studies in other specific indications and to seek approval for a wider label for Feraccru whilst continuing to focus on the specialist prescribed segment.
- **Expansion into other specific indications** – Whilst the current pivotal Phase 3 Study data has been generated in IBD, the next Phase 3 study planned is in CKD. The Company does not intend specifically to target dialysis patients in relation to Feraccru,

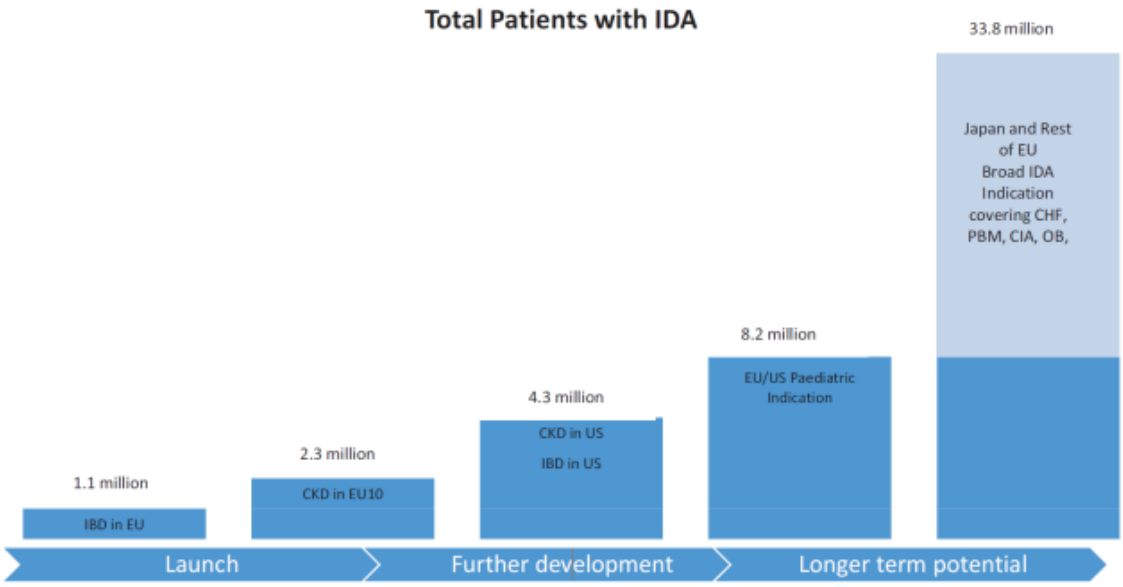
except in home dialysis where patients still need to present to hospitals for their routine iron supplementation therapy. This is intended to lead to an expansion of the Feraccru label.

- **Out-license in additional markets** – The Company will continue to explore opportunities to out-license the marketing rights for Feraccru in additional markets and in other geographies such as the Far East and BRIC countries. In addition, the Company is actively engaged in territory licence discussions in geographies in Europe where it does not plan to establish its own sales force.

Available patient population based on the Group's commercialisation strategy

Based on the above commercialisation strategy, the following table sets out the Directors' estimates of the total addressable market in terms of available patients with IDA suitable for Feraccru:

Figure 4. Company estimates of total patients with IDA



Feraccru pricing strategy

Feraccru is being positioned commercially as an effective alternative to IV iron. As a twice daily oral by comparison there are clear cost advantages associated with Feraccru, especially in patients who do not routinely present to hospital and IV products can only be administered in a ''hospital-like'' setting where resuscitation facilities are available.

Key features to pricing relevant to Feraccru's positioning include:

(a) It is well understood and generally accepted that an effective oral product should provide significant cost advantages for a payer when taking into account the total cost of IV iron administration and this should predispose payers to a positive discussion when considering Feraccru's pricing; and

(b) The latest generation of IV iron products have used earlier generations to successfully agree a relative premium price for these products compared to the earlier products on the basis of the savings from reduced administration time and frequency. Therefore pricing authorities have already accepted the inclusion of total administration costs when agreeing pricing, which should further facilitate Feraccru obtaining favourable pricing.

Whilst discussions with pricing authorities at the national level can only commence after MAA approval, detailed research (including specific EU and US payer research) has been undertaken by the Company that supports its pricing strategy. In addition, as noted in paragraph 4.5.2 below the Group is currently undertaking a Phase 3b trial in Europe which will provide pharmaco-economic data for use in pricing discussions both with national agencies where required and also at the local formulary level. This study is intended to demonstrate statistically significant non-inferiority data against the IV products that the

Directors believe to be the competition to Feraccru. This data, if forthcoming, and which the Company expects will be available during 2016, will support both negotiations with national and local reimbursement authorities and discussions with prescribers. The Directors believe this data will be helpful to the overall commercial proposition and to facilitate faster adoption of Feraccru. It will also assist in positioning Feraccru at a relatively similar price to the drug only cost of IV iron.

The Company has developed a phased launch plan that takes account of the need to seek reimbursement approval in certain countries either prior to launch (such as France, Spain and Italy) or within a period of time after launch (such as Germany).

Having had confirmation from the authorities in Germany (Germeinsamer Bundesausschuss-GBA) that Feraccru will not require AMNOG (Arzneimittelmarkt-Neuordnungsgesetz) review, this means the Company can set the list price of Feraccru at launch in Germany.

Launch strategy

The Company has developed a commercial plan to maximise the opportunity for premium pricing across the EU. In the core member states including the UK, Ireland, Germany, France, Italy, Spain and Benelux, the Company intends to commercialise Feraccru using its own central and field -based sales and commercial teams.

The UK and Ireland are planned to be the first launch countries in 2016 and planning for this is well underway with a UK General Manager having been appointed in December 2015. Having had confirmation from the regulatory authorities that Feraccru will not require AMNOG review, Germany is expected to be the second launch country later in 2016. This is intended to be followed by launches in Italy, France, Portugal and Spain in 2017.

In addition, territory licence partners are expected to launch in other countries through 2016 and 2017 based around the Company's own launch strategy.

A core commercial aim for Feraccru will be to influence the guidelines for the treatment of IDA by positioning Feraccru to be used for all OFP-intolerant patients before IV therapy. Initially this will be focused on patients who have IDA related to IBD.

Over the longer term, changing the treatment guidelines will form the basis of the Group's future market expansion work for Feraccru to be the primary choice for second line treatment in all causes of IDA.

The Company will also employ a strategy to educate primary care physicians so Feraccru's position is further underpinned.

Partner Distribution

As set out in paragraph 9.2 of Part 10 (*Additional information*) the Company already has a distribution agreement in place with IRORPH for certain Eastern European and Middle Eastern countries for Feraccru. The agreement runs for 5 years from MAA approval, with AOP holding an option to extend for a further 15 years. In addition, early stage discussions have commenced with potential partners in other territories where the Company does not intend to establish its own sales force.

4.5 Research and Development, Patents and Licences

4.5.1 Completed clinical trials

The Group has conducted a number of studies with Feraccru since acquisition. The most significant was the pivotal Phase 3 Study, which commenced in mid-2011 and completed in 2014. The Group is currently conducting a randomised Phase 3b study comparing Feraccru with a leading IV iron (ferric carboxymaltose). This study is not required for regulatory approval of Feraccru by the EMA but is intended to provide further safety and efficacy data, pharmaco-economic data and non-inferiority data, all of which will support the commercial positioning and launch of Feraccru.

Future studies are planned to generate pivotal data in other indications and to provide additional safety data to enable the Company to expand its regulatory approvals initially into the US and then into other geographies and indications. These are discussed further in paragraph below.

Clinical studies conducted before acquisition

Prior to SHG's acquisition of Feraccru from Vitra Pharmaceuticals in early 2010, a series of clinical studies with Feraccru were conducted in both healthy subjects and IDA patients (with and without IBD). The studies have provided a considerable body of knowledge on the absorption, efficacy, safety and tolerability of a range of doses of Feraccru.

Clinical studies conducted after acquisition

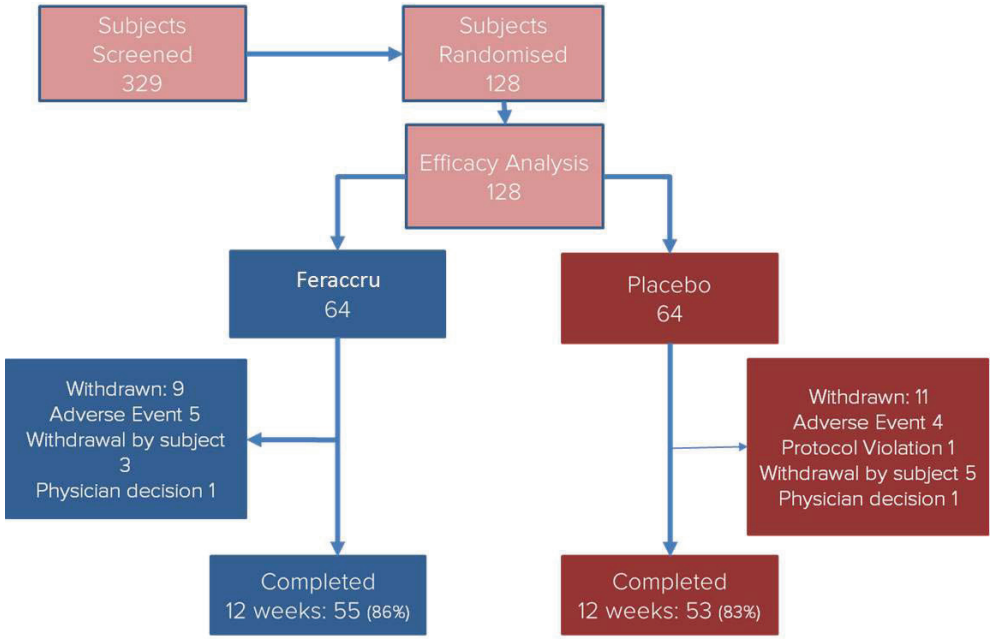
Following the acquisition of Feraccru by SHG, the Group has conducted three main clinical studies. The primary objective of these studies was to evaluate the pharmaco-economic profile and the pharmacokinetics, safety and efficacy of Feraccru. The key study that was conducted was the pivotal Phase 3 Study of safety and efficacy.

Pivotal Phase 3 Study

The Group designed the pivotal Phase 3 Study, which was conducted in 128 patients (64 to treatment and 64 to placebo) to compare Feraccru to placebo in two separate arms, Ulcerative Colitis and Crohn's disease. The pivotal Phase 3 Study was a safety and efficacy study with an initial 12-week double-blind phase followed by a 52-week open-label phase.

Efficacy was evaluated over the first 12 weeks of randomised treatment. Patients had all failed treatment on OFPs and had mild and moderate IDA with haemoglobin levels of $>$9.5g/dL on screening. All completed subjects from the randomised phase, where eligible, received open-label Feraccru for up to an additional 52 weeks.

Figure 5. Details of the subject disposition of the pivotal Phase 3 Study.



The results of the double blind phase showed compelling efficacy compared to placebo, with a "placebo-like" safety profile, and the open label phase further showed an additional small continuation in the increase in Hb over time. Iron stores continue to be replenished over the full 64-week treatment period.

Further details of the results of the pivotal Phase 3 Study are outlined below.

Efficacy results

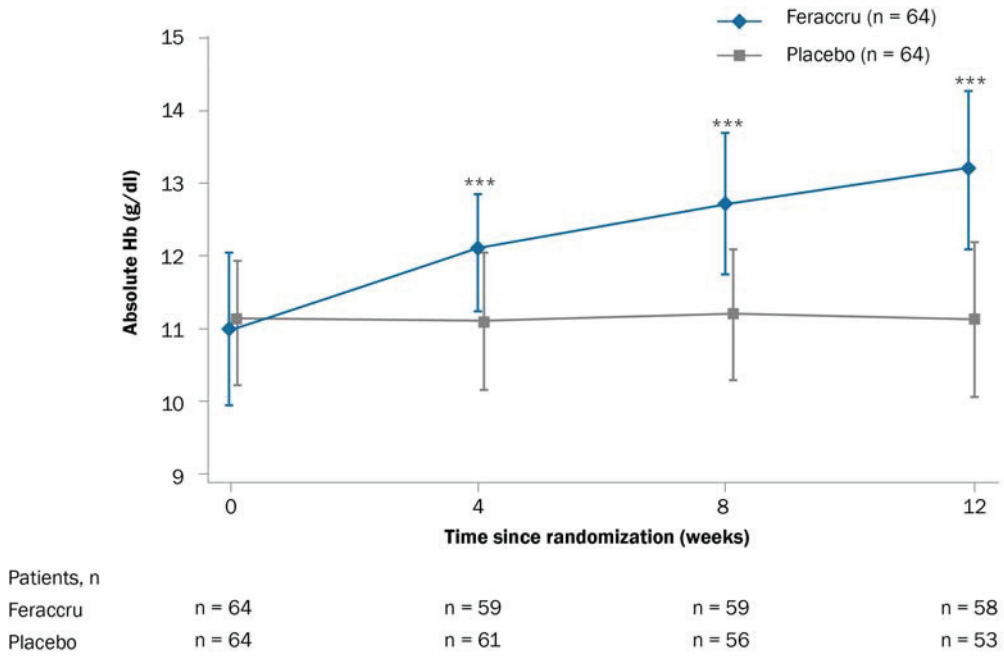
The results of the 12-week period of the pivotal Phase 3 Study were published in Inflammatory Bowel Disease, 2014 and presented at the European Colitis and Crohn's Organisation meeting in February 2014.[23] In terms of the primary endpoint, in Feraccru subjects there was a mean overall improvement in Hb levels of 2.25 g/dL compared to

23 Gasche C et al. 2014. Correcting Iron Deficiency Anaemia in IBD: A Pivotal Phase 3 Study of a Novel Oral Ferric Iron; Gasche C et al. 2014. Inflammatory Bowel disease.

baseline. In contrast, mean Hb levels in placebo subjects were virtually unchanged (11.10 g/dL at baseline and 11.13 g/dL at week 12). The mean improvement in Hb levels delivered by Feraccru was statistically significantly ($p < 0.0001$) compared to placebo.

Feraccru therefore met the primary efficacy endpoint of change in Hb concentration after 12 weeks of treatment compared to placebo. This mean overall improvement in Hb levels can be considered a highly, clinically meaningful change.

Figure 6. Primary efficacy endpoint for Feraccru-01-301 & 302 study



Feraccru met all key secondary efficacy endpoints (compared to placebo), including:

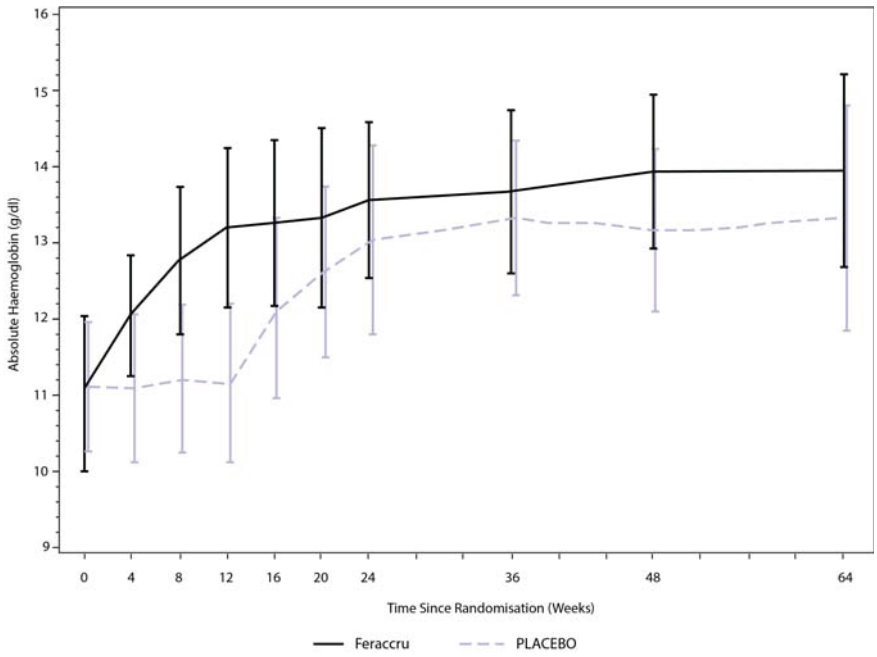
- Achieving at least an increase of 1 g/dL from baseline Hb concentration at Week 12;
- Achieving at least an increase of 2 g/dL from baseline Hb concentration at Week 12;
- Achieving normalised Hb concentration at Week 12); and
- Achieving improved Hb concentration at Weeks 4 and 8 ($p < 0.0001$).

In addition, in patients with low starting haemoglobin levels ($>10 - <11$ g/dL and $>9.5 - <10$ g/dL), Feraccru showed a mean improvement in Hb levels at 12 weeks of 2.39 g/dL and 3.48 g/dL respectively, compared to the baseline.

Long-term and other results of the pivotal Phase 3 Study

When the placebo subjects were transferred to Feraccru treatment in the open-label phase, there was a sharp rise in Hb levels that mirrored the response in the Feraccru group in the double-blind phase. There was further increase in Hb up to 48 weeks of treatment and no indication of any reduction in efficacy over the full 64-week treatment period. As outlined in the below table, long-term treatment with Feraccru resulted in Hb normalisation in greater than 80% of patients.

Figure 7. Efficacy over 64 weeks for both treatment groups: Feraccru and Placebo

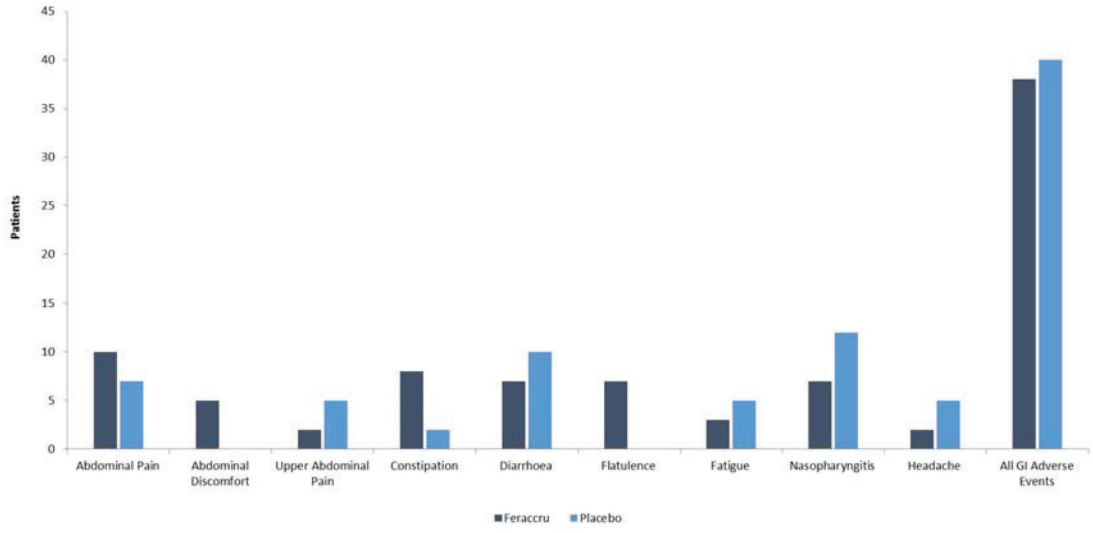


Error bars show 1 standard deviation from the main.

Safety and tolerability

Feraccru has a good safety profile. The proportion of subjects reporting AEs in the double-blind phase was lower in the Feraccru group than in the placebo group. As expected in an IBD population, GI-related AEs were the most common, with similar proportions of subjects reporting GI events in both treatment groups. Importantly, data indicated that Feraccru did not exacerbate IBD symptoms over the 12-week treatment period. The rate of AE's and related AE's were low and similar in both treatment groups: flatulence, constipation and abdominal discomfort/distension occurred slightly more frequently following Feraccru administration. No Serious Adverse Events were reported which were attributable to Feraccru.

Figure 8. All AEs occurring in at least 5% of subjects



Data from the longer-term open-label phase confirmed the generally benign safety profile of Feraccru demonstrated in the double-blind phase. There was no indication of any increase in frequency or severity of AEs with duration of treatment.

Pharmacokinetics study

Following the pivotal Phase 3 Study, the Group conducted an open-label, randomised, multiple dose pharmacokinetics ("PK") study in 24 subjects with iron deficiency (with or without anaemia). The primary objective of the PK study was to evaluate the kinetics of maltol, as well as iron uptake in the blood and urine, after single and repeated oral doses of three different dosages of Feraccru. Maltol showed predicable pharmacokinetics with linear increases in exposure. The maltol was rapidly metabolised to maltol glucuronide and excreted in the urine. Total serum iron increased with increasing dose, however the increase was not proportional. Results of the study suggest a dose higher than 30mg twice daily may be an effective option, although further patient studies are required. The PK study formed part of the MAA.

The results of the study led to a further patent application for the higher dose, P014. For further details please refer to Part 7 (*Patent Agent's Report*).

4.5.2 Current and future clinical trials

Phase 3b comparator study

This clinical study is designed as a non-inferiority trial comparing the efficacy and safety of Feraccru to the market-leading latest generation form of IV iron (Ferinject, ferric carboxymaltose). It will also generate a range of pharmaco-economic endpoints to support the Company's commercial activities.

As with the Phase 3 Study, this study is for the treatment of IDA in patients with IBD. It is a randomised, controlled, international multicentre study that is being conducted in Germany, Belgium, France and Spain with approximately 240 subjects randomised 1:1 Feraccru to Ferinject. Patients with starting haemoglobin levels below 9.6 g/dl (but above 7.5 g/dl) will be eligible for enrolment in this study. It is anticipated that data from the initial 12-week phase of the study will be available in late 2016, with the complete 52-week efficacy, safety and pharmaco-economic data available in late 2017.

The Directors' believe that the probability of Feraccru demonstrating non-inferiority to intravenous iron from this study is relatively high for a number of reasons including but not limited to (i) it is being conducted in a patient population that has already demonstrated a clear and positive response to Feraccru therapy over both 12 and 64 weeks; (ii) patients with lower Hb levels are being recruited and Feraccru has historically demonstrated a bigger and faster response in such patients; (iii) the primary endpoints of this study have already been demonstrated by Feraccru in earlier studies; (iv) it is a non-inferiority study rather than a superiority study and (v) the non-inferiority study is powered to 90% which means that there is a 90% chance that any difference which is detected in the relative effectiveness of Feraccru and the IV comparator also exists in the wider population.

Phase 3 CKD study

This is intended to be undertaken as a randomised, placebo controlled multi-centre study comparing Feraccru to placebo in patients with CKD. The study is expected to be of a broadly similar size to the previous Phase 3 Study in IBD conducted with approximately 195 patients. Whilst the majority of subjects are expected to be recruited in the US, the Company is considering an element of recruitment to this study in Europe.

Paediatric Plans

The Group's agreed European Paediatric Investigation Plan ("PIP") anticipates the following key studies to be conducted with Feraccru in the paediatric population:

(a) Pharmacokinetic Study: A limited open-label randomised multiple dose trial to evaluate pharmacokinetics and tolerability in children and adolescents with iron deficiency between 10 and 18 years old with at least 36 subjects randomised. Planning for this study has commenced.

(b) Phase 3 study: A Phase 3 study in all indications with IDA comparing Feraccru with oral ferrous sulphate in children from 6 months to 18 years with at least 49 patients per arm for at least 12 weeks of treatment. This study will commence once the Pharmacokinetic Study has completed.

Further studies

In the longer term, the Company intends to conduct further studies to generate additional clinical data for Feraccru in a number of other indications where IDA is a significant problem, including women's health, CHF, anaemia in surgery and oncology.

The Company does not intend to test superiority of Feraccru to IV iron. In GfK's view, only superiority to placebo and non-inferiority to IV Iron are pertinent in the context of Feraccru and neither the Company or GfK consider it necessary for Feraccru to demonstrate superiority vs IV iron.

4.5.3 Regulatory Strategy

Key features of the regulatory strategy in respect of Feraccru include:

(a) The use of a suitable regulatory approval pathway to allow the Company to make use of, and reference, existing third party published data (in particular non-clinical safety data) in respect of the constituents of Feraccru, including maltol and ferric iron;

(b) Submission of a full data package containing proprietary information generated from non-clinical studies and clinical trials and its own quality package to support the MAA/NDA applications allowing the Company to take advantage of data and marketing exclusivity provisions in both Europe and the US; and

(c) Centralised filing in Europe (see below).

Interactions with Regulatory Authorities

The Company has conducted regular interactions with the regulatory authorities in Europe and the US throughout the development process in order to create the optimal pathway to regulatory approval. A summary of these interactions to date is as follows:

Agency	Date	Topics discussed
MHRA (UK)	September 2010	Non-clinical, clinical and regulatory
	June 2011	CMC, non-clinical, clinical and regulatory
	February 2013	Clinical and regulatory
BfArM (Germany)	September 2011	CMC , non-clinical and regulatory
	February 2013	Clinical and regulatory
	July 2014	MAA Pre-submission meeting
EMA	February 2014	MAA Pre-submission meeting
	November 2015	MAA oral hearing
	December 2015	CHMP recommendation for Feraccru to receive marketing authorisation
AEMPS (Spain)	July 2014	MAA Pre-submission meeting
FDA	May 2012	Pre-IND meeting to discuss US development plan

Centralised Application

Feraccru does not belong to a category of product that has mandatory access to the Centralised Procedure that results in a single Pan-European marketing authorisation.

The EMA can however grant access to the Centralised Procedure for products where the product constitutes a significant therapeutic, scientific or technical innovation, or the granting of a Community authorisation for the medicinal product is deemed to be in the interests of patients at Community level.

The EMA confirmed that Feraccru is eligible for submission under the centralised procedure on the grounds that approval is ''in the interests of patients at Community level''.

Marketing Authorisation Application in Europe

The Company submitted its Marketing Authorisation Application (''MAA'') to the EMA in December 2014. On 17 December 2015 the CHMP unanimously adopted a positive opinion that Feraccru be granted a marketing authorisation in all member states of the European Union. This marketing authorisation is scheduled to be issued in the first quarter of 2016.

Details of the agreed indication for the Marketing Authorisation

The indication for Feraccru has now been agreed with the EMA. The indication is as follows:

Feraccru is indicated in adults for the treatment of IDA in patients with Inflammatory Bowel Disease (IBD).

Specific reference is made in the indication to the clinical section of the Summary of Product Characteristics (SmPC) which sets out the summary phase 3 clinical data including the inclusion criteria that all patients enrolled had discontinued from prior OFP treatment.

Consistent with the Group's commercial strategy, the indication approved label will enable the Group initially to target IBD patients with IDA who are recognised by payers and practitioners as the hardest to treat population with existing oral therapies with highest inherent intolerance to OFPs. As per the clinical trial protocols, the Company does not initially expect Feraccru to be licensed in patients with inflammatory bowel disease (IBD) flare or in IBD-patients with haemoglobin (Hb) $<$9.5g/dl, although future clinical trials may make this possible. For further details of the Group's strategy in relation to Feraccru refer to paragraph 4.4 of Part 2 (*Information on the Company and the Group*) of this document.

US approval

Based on guidance received in 2013 from the FDA, a larger safety database than has been generated by the Phase 3 IBD study is likely to be required to obtain marketing approval in the US. In order to generate the additional data, and to support a wider label in the US beyond IDA in IBD, the Company intends to conduct a Phase 3 study in CKD to generate both efficacy and safety data. These additional data will be combined with the existing data used to obtain EU marketing approval and the ongoing phase 3b study to provide a comprehensive package for review.

Expansion of Feraccru approval to other jurisdictions

The Group intends both on its own account and, where appropriate, with partners, to expand the regulatory approval and therefore the commercial opportunity for Feraccru in other jurisdictions. This would include countries where the Group is eligible for accelerated approval procedure following EU approval and other countries where a fully independent review is required (e.g. Japan).

Paediatric Plans in the EU

The Paediatric Investigation Plan (''PIP'') in the EU was approved by the EMA in September 2013. In the opinion of the Directors, the requirements in respect of obtaining a paediatric approval for Feraccru, which have been approved by the Paediatric Committee of the EMA (''PDCO'') are not onerous and are achievable over a realistic timeline following MAA approval. The requirements for paediatric approval for Feraccru are as follows:

(a) creation of an age-appropriate powder for suspension formulation;

(b) a limited pharmacokinetic study in children aged between 10 and 18 years; and

(c) a safety and efficacy (Phase 3) study comparing Feraccru to ferrous sulphate with at least 49 patients per arm in children between 6 months and 18 years with descriptive statistics only.

Paediatric Plans in the US

Prior to the submission of Feraccru for marketing approval, the Group will look to develop a paediatric plan in the US based on the agreed EU PIP and precedent with other IDA therapies. The Directors believe that the paediatric plan is likely to be similar to that agreed in the EU.

4.5.4 Medical Affairs Strategy

The Company's medical affairs strategy will be essential in establishing peer to peer dialogue regarding both Feraccru and iron deficiency. This dialogue will aid appropriate positioning of Feraccru in treatment and reimbursement guidelines both internationally and at a local level. Aligned fully with our commercial strategy the Company's medical affairs team will educate clinicians and payers on Feraccru and its uses in treatment pathways. Examples of some of these engagements are outlined below.

Engagement and interactions with Key Opinion Leaders (''KOLs'')

The Group has constantly and effectively engaged and interacted with KOLs and influencing clinicians in respect of IDA in IBD. These interactions started as part of the consultations for the design of the pivotal Phase 3 Study and continue in respect of further clinical research, publications and symposia.

For further details of the experts and opinion leaders who have been involved in the development of Feraccru or PT20 and/or the related clinical and non-clinical trials please refer to paragraph 10.4 of Part 1 (*Key Information and Details of the Placing*).

Publication of clinical data in journals

To date the Group has published the following peer review journals:

- Inflammatory Bowel Disease, 2014: ''Ferric Maltol is Effective in Correcting Iron Deficiency Anaemia in Patients with Inflammatory Bowel Disease: results from a Phase-3 Clinical Trial Program'' (Professor Chistoph Gasche et al.).
- Drug Discovery Today, August 2015**:** ''Addressing unmet need in Inflammatory Bowel Disease'', Dr Bernd Bokemeyer, M.D.
- Expert's Opinion on Pharmacotherapy, November 2015: ''Ferric maltol (ST10): a novel oral iron supplement for the treatment of iron deficiency anemia in inflammatory bowel disease'' (Andreas Stallmach et al.).

Publication of abstracts

To date the following abstracts have been presented by the Group:

- ECCO, 2014: Abstract/Poster: Feraccru-01-302 top-line efficacy results.
- Digestive Disease Week (''DDW''), 2015: Abstract/Poster on efficacy and long term safety data from Feraccru-01-301&302.
- DDW, 2015: Abstract/poster on Feraccru-01-101 PK study.
- United European Gastroenterology Week (''UEGW''), 2015: Abstract/poster accepted for inclusion and this includes additional data and analysis for the pivotal Phase 3 Study. Authored by Dr Brunning.

Symposia and presentations

The following symposia and presentations have been conducted by the Group:

- ECCO, February 2014: Presenting the results of the pivotal Phase 3 Study by Tariq Ahmad.
- ECCO, February 2015: The Company ran a symposia attended by approximately 100 participants chaired by Professor Gert von Ashe entitled ''Looks can be deceiving, all oral irons are not the same'' to discuss the relative merits of Feraccru.
- UEGW, October 2014: Presentation of the clinical efficacy data for the pivotal Phase 3 Study by Professor Stallmach.
- UEGW, October 2015: Sponsorship of an educational symposium agreed in October 2015.

Influence on published guidelines for the treatment of IDA

As noted above, ECCO and other organisations have published guidelines for the treatment of IDA in IBD in Europe and elsewhere. The Company has been seeking, and will continue to seek, to influence the guidelines to ensure Feraccru is included as a clear therapeutic option ahead of IV in patients who have failed treatment on OFPs or for whom such treatment is unsuitable.

The original ECCO Guidelines were published in 2007 and co-authored by Professor Christoph Gasche, one of the Company's scientific advisors, lead investigator in the pivotal Phase 3 Study and lead author of the subsequent peer-reviewed scientific paper. In January 2015, the European Consensus on the Diagnosis and Management of Iron Deficiency and Anaemia in Inflammatory Bowel Diseases referenced Feraccru as follows: ''*Preliminary data on novel ferric formulations such as ferric maltol (Feraccru) indicate effectiveness with a*

preferred adverse event profile, even in IBD Patients with a history of intolerance to ferrous sulphate".[24] Professor Gasche and another of the Company's scientific advisors, Dr Tariq Iqbal, both co-authored this report.

With an approved product to hand the Company will continue to develop Feraccru's Medical Affairs strategy both on an international and national level as it develops additional clinical data and builds its team of Medical Science Liaisons.

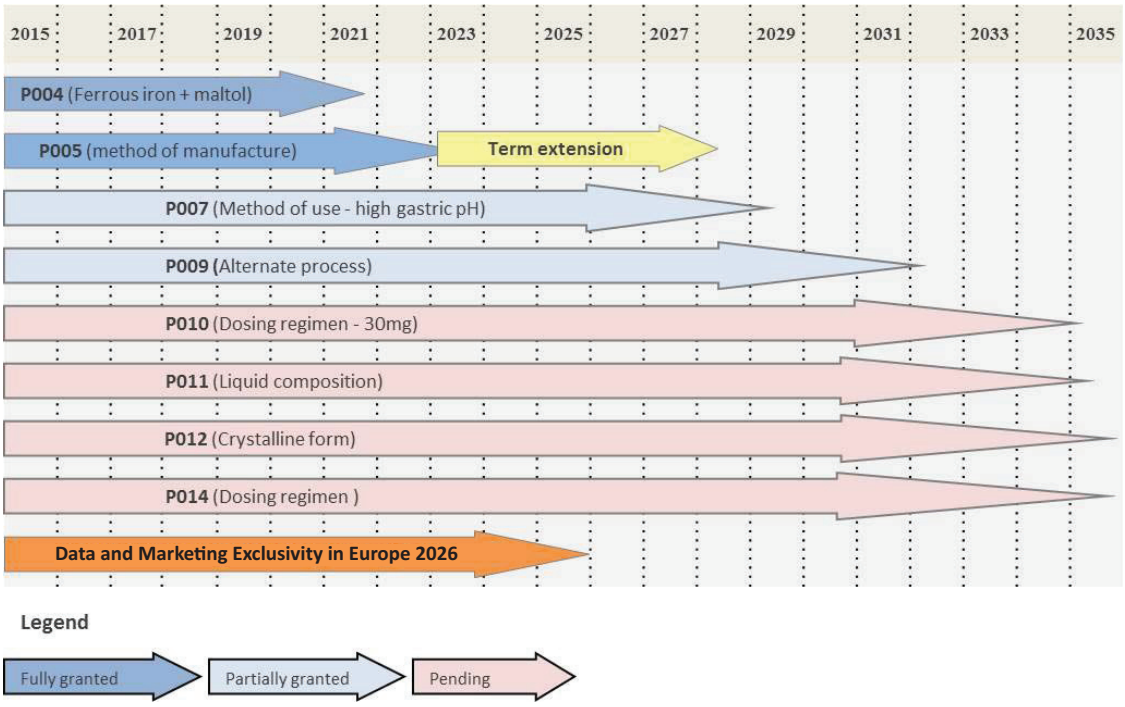
4.5.5 Intellectual Property and Data and Marketing Exclusivity

Patents

Overview of the Feraccru patent portfolio

The Group has robust and comprehensive patent protection relating to Feraccru. The Group's patent portfolio comprises granted patents and patent applications covering Feraccru's method of manufacture, medical use, crystalline form, liquid formulation and intended treatment regime, providing valuable protection for specific aspects of Feraccru and its use.

The chart below has been extracted from the Patent Agent's Report in Part 7 of this document. The chart summarises the terms of the key patent families, as well as data and marketing exclusivity in Europe, for Feraccru:



Patent term expiry in the US may differ from the above by a matter of months. Please see the Patent Agent's Report in Part 7 of this document for further details.

The Group's patent portfolio for Feraccru consists of 9 owned patent families, which were either acquired from Vitra Pharmaceuticals in 2010 (and subsequently prosecuted or maintained by the Group) or filed by the Group itself. All patents and patent applications described in this paragraph 4.5.5 are wholly owned by the Group.

The Group's key granted patent covers the core manufacturing process for Feraccru (patent family P005). This patent family includes granted European patents (covering nine countries in Europe) as well as granted patents in the US and Canada. These patents initially continue until 2023 but the Group intends, following grant of marketing authorisations for Feraccru in Europe and the US respectively, to apply for a patent term extension in relation to both the European and US patents in this family, in order to further extend patent protection by up to five years to 2028. A further paediatric extension may also be possible.

24 Dignass AU et al. European Consensus on the Diagnosis and Management of Iron Deficiency and Anaemia in Inflammatory Bowel Disease. J Crohn's and Colitis, 2015, 1-12

Notably, patent family P005 protects the Group's method of manufacture of Feraccru, which possesses significant advantages over all other (less efficient) manufacturing methods in terms of yield and purity of the resulting product.

The Group also owns a series of blocking patents, which cover alternative methods for manufacturing Feraccru (patent families P001 and P009). These patents prevent competitors from "designing around" the core manufacturing process covered by patent family P005 and therefore further support the IP protection for Feraccru.

Other granted patents owned by the Group include medical use patents (patent family P007). This patent family covers the use of Feraccru for treating IDA patients with a gastric pH of 4 or above. Patents have been granted in Australia, China, Japan, Hong Kong and Singapore and are pending in other territories including Europe and the US. The patents in this family provide protection until 2029.

In addition to the patent families acquired from Vitra Pharma, the Group is pursuing new patent applications with a view to further strengthening the IP protection surrounding Feraccru. The Group intends to prosecute these applications in all major pharmaceutical markets. The recent applications (all of which are currently awaiting publication or otherwise pending grant) cover the following:

(a) Crystalline form of Feraccru (patent family P012): if granted, this patent will provide key composition of matter protection for Feraccru in the crystalline form in which it is intended to be sold by the Group, to 2035.

(b) Treatment regimens (patent families P010 and P014): these patent families cover current and potential dosing regimens for Feraccru.

(c) Liquid formulation of Feraccru (patent family P011): this patent application covers a composition relevant for paediatric and other patient groups where a different (e.g. liquid) formulation of Feraccru is required (such as in cases of patients with dysphagia).

In addition, if granted, patent families P007, P010, P012 and P014 will be Orange Book listed in the US, providing additional protection. Any generic company that intends to make or sell a drug which arguably infringes a patent listed in the Orange Book must notify the patent owner. If the patent owner files a claim for patent infringement then a 30-month stay before the generic company can sell the allegedly infringing drug shall be granted, subject to FDA approval. Further detail regarding Orange Book listing is set out in the Patent Agent's Report prepared by Stratagem and included as Part 7 (*Patent Agent's Report*) of this document.

The Company is actively considering further patenting opportunities for Feraccru and plans to file further patent applications where appropriate. For further details on the existing patent families relating to Feraccru, please refer to the Patent Agent's Report prepared by Stratagem and included as Part 7 (*Patent Agent's Report*) of this document.

Data and marketing exclusivity

In addition to patent protection, Feraccru will benefit from data and marketing exclusivity in Europe and the US.

Upon the approval of Feraccru by EMA, the Directors believe that Feraccru will benefit from 8 years of data exclusivity before a competitor can rely on the Group's non-clinical or clinical data to apply for a marketing authorisation for a competing product and a further 2 years of marketing exclusivity before any such product may be placed on the market in Europe. An additional one-year's exclusivity may be obtained in a number of circumstances, such as where the Group is granted a marketing authorisation for a significant new indication for Feraccru. Assuming Feraccru is approved in Europe in 2016, the Group will therefore have marketing and data exclusivity for Feraccru in Europe until 2026.

The current development and registration strategy for Feraccru in the US will deliver 3 years of data exclusivity following approval of Feraccru by the FDA.

Patent freedom to operate

The Group has conducted a number of Freedom to Operate searches through its appointed patent agents, the most recent of which was undertaken in July 2015.

These searches did not identify any third party filed patents, which, in the opinion of the Directors, would inhibit the Group's ability to produce and commercialise Feraccru.

Trade marks

The product name FERACCRU is protected as a registered trade mark both in the UK and across the European Community. Further details of these registrations are set out in the table below:

Trade mark	Territory	Registration no.	Status
FERACCRU	UK	3059741	Registered
FERACCRU	European Community	12995486	Registered

4.5.6 Development efforts

The Group has undertaken a great deal of development work since the acquisition of Feraccru. The Group has had extensive engagement with the regulatory authorities in both Europe and the US in planning its historical and future clinical trials and the EMA and the FDA have approved the designs of the clinical trials undertaken by the Group to date. The Group has undertaken a number of successful non-clinical and clinical trials, including the pivotal Phase 3 Study of Feraccru.

4.6 Manufacturing and supply chain

Feraccru is currently manufactured on behalf of the Company by Piramal, a leading provider of clinical services and commercial manufacturing to the global pharmaceutical industry. Piramal is responsible for manufacture of Drug Substance and Drug Product, labelling, final packaging and all the associated analytical and laboratory testing. The Group has been working with Piramal since acquiring Feraccru in 2010. Piramal has been contracted to produce sufficient commercial batches of Feraccru in time for planned launch. The Group has also worked with a number of additional specialist vendors in respect of certain aspects of the manufacturing development.

The Group has a manufacturing supply agreement in place with Piramal which will not expire before delivery of initial commercial supplies. This is a development contract that has provided the contractual basis for their work with the Group to date, including the supply of launch stocks. The Group is currently negotiating a manufacturing agreement with Piramal for the long-term supply of Feraccru from its site in Morpeth, UK. In addition, as is usual in the industry, the Company is currently engaged in a process to approve a second European-based supplier of Feraccru to provide a dual-source supply.

In preparation for launch, the Company is in advanced discussions with service providers to provide distribution capabilities in the major EU markets, initially focused on the UK as first launch market. In addition, the process of applying for the appropriate licences from national authorities, including a Wholesale Dealer Licence (WDL) from the MHRA, is underway.

Drug Substance Development

Feraccru has been manufactured by several different processes over the extended programme covering the initial clinical evaluation of the product from the late 1990's – prior to acquisition by the Group – to date. These early processes were unsuitable for industrialisation, due to unacceptable levels of impurities, the use of organic solvents, challenges in manufacture and the costs to manufacture. Following the development of new manufacturing methods by Vitra Pharmaceuticals, the patents relating to which are now owned by the Group, the latest phase of process development employs a wholly aqueous process that produces a highly pure product that meets current regulatory standards and enables cost-effective and technically feasible scale-up and use of industrial plant processes. This process was used by SHG for its clinical trial supplies and will be employed, with suitable optimisation, going forward.

Raw Material Sourcing

The Group sources its registered starting materials through its manufacturing supply arrangements with Piramal. However, it has had direct input into the selection of key starter material vendors. The key ingredients for Feraccru are provided by approved suppliers Apiscent Inc. based in Wisconsin, US (using an FDA and EMA approved facility) and Jost Chemical Co. St Louis, Missouri. Both starting materials have detailed specifications for

acceptable levels of impurities before onward shipment to Piramal for use in the manufacture of Feraccru. Whilst relationships with the current suppliers are good, the Directors are satisfied that a number of suitable alternative suppliers are available.

Manufacturing costs

The costs of the starting materials required for the production of Feraccru are low and the patented manufacturing process is neither expensive nor overly complex. As a result, this provides for an inherently low cost of goods.

In the longer term, the Company has the potential to seek additional manufacturing efficiencies from:

(a) Approval of offshore higher volume for either or both of Drug Substance or Drug Product in a suitable location such as China or India.

(b) Development of a tablet formulation to replace the existing encapsulated product.

(c) Development of new supply arrangements for starting materials from higher volume, lower-priced supplier(s).

4.7 Competition

Feraccru is initially to be targeted at adults with IDA and IBD who have failed treatment on OFPs or for whom such treatment is unsuitable. Accordingly, the Directors do not therefore regard current OFPs as direct competitors. There is one existing oral ferric compound that the Directors are aware of, being oral ferric polymaltose and one potential product, IHAT (iron hydroxide adipate tartrate) that is in the very early stages of development.

Oral ferric polymaltose is sold by Galenica through its subsidiary Vifor Pharma under the brand name Maltofer as a chewable tablet or syrup. It was launched in 1978 but is not commercially available in the world's major prescription pharmaceutical markets.

The Directors do not anticipate further approvals for marketing being sought in respect of Maltofer as a pharmaceutical product in Western markets due to its relative lack of efficacy due to low levels of absorption. In 2014, Galenica reported sales of Maltofer of CHF 50.5m (approximately £33.4m).

IHAT is a ferric-iron based research-stage product that has been under initial development by the MRC in the UK. In a recent study that compared IHAT to ferrous sulphate in 26 premenopausal women with mild to moderate iron deficiency, IHAT was only 80% as efficient as current ferrous iron supplements at replenishing haemoglobin.[25] Considering the very early stage of development and the initial indication of efficacy being lower than OFPs, the Directors do not consider this product currently presents a significant competitive threat.

Commercially Feraccru is being targeted initially as a treatment for IDA patients with IBD who have failed treatment on OFPs or for whom such treatment is unsuitable and whose only current treatment option is intravenous iron therapy. Accordingly, IV iron is regarded by the Directors as being the main competitor.

First generation IV iron infusions – High molecular weight dextran

The first IV iron products were high molecular weight iron dextrans such as Imferon, which was owned by Fisons plc. This was withdrawn from the market in the mid-1990s due to the high risk of anaphylaxis.

Second generation IV iron infusions – Low molecular weight dextran

These products were developed to try to reduce the high level of side effects experienced with high molecular weight dextrans. These started to get approval in the mid to late 1990s and products included:

- Dexferrum (US only)(Galenica)
- INFeD (Allergan)
- CosmoFer (Pharmocosmos)

25 Powell, J, Bruggraber, S, Faria, N, Poots, LK, Hondow, N, Pennycook, TJ, Latunde-Dada, G, Simpson, R, Brown, AP & Pereira, DIA 2014, 'A nano-disperse ferritin-core mimetic that efficiently corrects anemia without luminal iron redox activity' Nanomedicine., 10.1016/j.nano.2013.12.011.

- Ferrlecit (sodium ferric gluconate)

The second generation products are not widely used having been overtaken by later generation IV products.

Third generation – Iron sucrose and Iron Isomaltoside

In the late 1990s a new class of IV Iron products were introduced. These included:

- Venofer – iron sucrose (Galenica). This has become the standard of care in DD-CKD (a market which Feraccru is not planning to target specifically). This is being replaced in other indications by Ferinject through Galenica's endeavours to migrate patients from Venofer to Ferinject outside DD-CKD.
- Iron sucrose similar (generic forms of Venofer). There are a limited number of generic equivalents to iron sucrose approved nationally in the EU and in Asian markets. Despite Venofer being off patent for some time this is a very limited market due to the difficulty competitors have found in showing bioequivalence and hence obtaining approval. There is currently no iron sucrose generic approved in the US.

The latest generation IV products have sought to overcome the need for multiple infusions to administer IV iron inherent in the third generation products.

Fourth generation – High dose IV, faster administration

The latest generation of IV iron products are either IV ''push'' or sub-cutaneous injection and these were introduced to reduce the administration time and also increase the dose per infusion. The two key products in the market are:

- Ferinject (Galenica) -Ferric carboxymaltose. This was launched as Injectafer in the US in 2013 after approval in the EU in 2007. Ferinject has seen rapid recent growth both due to the switching of patients outside DD-CKD from Venofer to Ferinject but also as Galenica has sought to promote the better education, diagnosis and treatment of IDA in a number of serious diseases and in areas such as elective surgery where IDA is a routine problem. The Directors believe this significant educational effort and awareness raising by Galenica amongst potential prescribers of iron therapies will be of assistance to Feraccru.
- Feraheme/Rienso. Feraheme was launched in the US in 2012. It was initially approved for use purely in DD-CKD. Launched in Europe in 2013 by Takeda, it was withdrawn from the European market in March 2015 after the EMA introduced restrictions due to concerns regarding the potential side effects.
- Monofer (Europe only) – Iron Isomaltoside (Pharmocosmos). Monofer is a relatively high dose infusion IV treatment administered via an IV injection where oral iron preparations are ineffective or cannot be used or where there is a clinical need to deliver iron rapidly.

Of the above, the Directors regard Feraccru's principal competitors to be Ferinject (Injectafer) and Monofer. As set out in ''current and future clinical trials'' above the Phase 3b non-inferiority study currently being conducted in four countries in the EU utilises Ferinject as the comparator IV product.

5 PT20

5.1 Overview

Elevated phosphate in the blood is a ubiquitous complication of moderately and severely reduced kidney function. Evidence suggests that this metabolic disturbance is associated with increased cardiovascular morbidity and mortality.[26] Efforts to treat the condition with dietary restrictions, dialysis and the current generation of phosphate binders have had mixed success. Data from a large international study suggest that approximately 60% of all dialysis subjects have phosphate above the recommended value of 5.5 mg/dL.[27]

26 Kendrick J, Kestenbaum B and Chonchol M. Phosphate and Cardiovascular Disease. Adv Chronic Kidney Dis. 2011 March; 18(2): 113-119. doi: 10.1053/j.ackd.2010.12.003.

27 Emmett M. A comparison of calcium-based phosphorus binders for patients with chronic kidney disease. Dialysis & Transplantation, 2006.

5.2 *Current Treatment Options*

Dialysis

Current dialysis methods, whilst having a small positive impact on serum phosphate levels, do not alter these levels in a material way and it is believed a long dialysis time (up to 12 hours and beyond) would be required for this option to be effective.[28]

Calcium and non-calcium based phosphate binders

As preventative measures are largely ineffective, the standard of care for phosphate control remains the prescription of phosphate binders. The phosphate binders are taken with meals and act in the gut to bind phosphate and prevent its absorption into the bloodstream.

The three categories of phosphate binders currently commercially available are calcium-based phosphate binders (calcium carbonate and calcium acetate), polymer based phosphate binders (sevelamer) and metal-based phosphate binders (such as lanthanum carbonate, aluminium and iron).

While these phosphate binders have similar efficacy, they differ substantially in their associated side effects. Calcium-containing phosphate binders have been associated with raised calcium in the blood, increased bone weakness, progressive vascular calcification and increased mortality. Sevelamer is only modestly potent, requiring 8-15 tablets per day. Though lanthanum carbonate appears to have superior potency to sevelamer, it is associated with significant gastrointestinal side effects and is systemically absorbed. Accordingly, there are concerns regarding long-term systemic toxicity.

Iron-based phosphate binders

It has long been know that iron oxides are suitable for phosphate binding. As currently available agents have significant toxicity and/or have limited phosphate binding capacity and/or require a high pill load, iron based binders may represent a new generation of treatments for hyperphosphatemia.

The ability of iron to bind phosphate from food in the gut and prevent its absorption is well known and has led to the recent development and approval of iron compounds as phosphate binders. Iron based binders are specific binders to phosphate and do not prevent the absorption of other micronutrients. Ferric iron based products appear to be tolerated in the gut potentially making them suitable for clinical development.

The approval of two iron-based phosphate binders demonstrates that iron-based binders, including ferric oxides, can achieve therapeutically relevant phosphate binding. For further details please refer paragraph 5.11 of Part 2 (*Information on the Company and the Group*) of this document.

5.3 PT20's technology

Iron oxide adipate (''PT20'') is a novel ferric iron-based phosphate binder specifically engineered to enhance its phosphate binding properties.

As PT20 is an iron-based binder, the Company prospectively included some descriptive assessment criteria on haematology parameters in the completed Phase 2 study. These explored the potential for PT20 to provide additional therapeutic benefit to dialysis patients with iron deficiency anaemia. Whilst the data suggest there may be a dual benefit of PT20 for patients with hyperphosphataemia, that is, providing a level of iron supplementation in adults as well as acting as a phosphate binder, these additional benefits related to iron parameters will be fully explored in the Phase 3 programme.

The manufacturing process of PT20 makes it a more efficient phosphate binder compared to iron oxide, a naturally occurring form of iron. The integration of adipic acid (''adipate'') to form PT20 increases the phosphate binding capacity by a factor of 3, compared to the unmodified iron oxide. The aim of this is that fewer tablets are required to lower phosphate to target levels in patients with CKD. The manufacturing process to integrate adipic acid is based on patented technology.

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28 Chazot C and Jean G. The advantages and challenges of increasing the duration and frequency of maintenance dialysis sessions. Nature Clinical Practice Nephrology (2008) 5, 34-44. doi:10.1038/ncpneph0979.

Adipic acid is a naturally occurring small organic molecule. It is used in the food and packaging industry and has a good safety profile. The adipic acid in PT20 is displaced by bound phosphate, and is absorbed through the gut, metabolised and is excreted. The manufacturing process of PT20 also results in particles of a very small size, which maximises the surface available for phosphate binding.

5.4 Market opportunity

Hyperphosphatemia is a serious and inevitable clinical consequence of the advanced stages of CKD. The hyperphosphatemia market is large and growing and is driven by the rise in CKD in Western populations, itself driven to a large extent by the rise in obesity and diabetes. For example, in the US the dialysis population is estimated to be growing at approximately 4% per year and there were 450,000 dialysis patients in the US in 2012.[29] GfK estimate the global market for phosphate binders to be approaching $2 billion.

Furthermore there is a trend away from earlier generation calcium-based phosphate binders due to their potential to add to the risk of cardiovascular disease.

In addition there is a large population of pre-dialysis CKD patients who are much less likely to receive treatment for hyperphosphatemia as the prescribing guidelines vary between Europe and the US for leading phosphate binders. As far as the Directors are aware there are currently no phosphate binders approved for use in pre-dialysis CKD patients in the US. This represents a very large potential market for a novel, safe and effective phosphate binder.

The US market

The US market for phosphate binders is much more evolved than most other Western markets for the following reasons:

(a) The overall prevalence rate for CKD is much higher in the US than in Europe.

(b) In the US, dialysis centres (typically operated by private companies) have a detailed monthly performance assessments which includes the measurement of serum phosphate for all patients receiving haemodialysis and are penalised for out of target performance. Accordingly, it is more likely that treatment will be managed more effectively.

(c) The US healthcare system is generally considered to be an early adopter of new generation products and older generation calcium-based phosphate binders, which are now largely generic, tend to be far less frequently prescribed due to the much publicised cardiovascular safety concerns.

(d) With respect to reimbursement, phosphate binders fall outside the ''cap'' or ''bundle'' applied to Medicare reimbursement for dialysis and fall under the normal co-pay reimbursement insurance codes. Further, the current generation of phosphate binders tend to be approved at a level allowing for routine prescription.

Net annual sales of current phosphate binders are at least $650m in the US and at least $1.3bn worldwide with at least 80% of US dialysis patients using phosphate binders to control phosphate levels. The Directors are targeting peak sales for PT20 in excess of £200m p.a.

The EU market

In the EU, although prevalence rates are currently lower than in the US, the market for hyperphosphatemia is still significant. In Europe, patients with hyperphosphatemia are more likely to be prescribed calcium-based phosphate binders. Where these drugs are contra-indicated, sevelamer or lanthanum carbonate are routinely prescribed. Although this is expected to change with the increasing focus on the side effects of calcium-based phosphate binders, the Company plans to market or license PT20 in the US initially.

Overall, whilst there are a number of phosphate binders in the market, the Directors believe there is a significant and attractive market for a novel, effective, safe and well tolerated phosphate binder and, in this patient population, early studies have indicated it will have the ability to be used with a relatively low pill burden. PT20 has demonstrated promising evidence that it can fulfil these requirements and this will be explored further in the Phase 3 pivotal programme, which is expected to be funded from upfront payments achieved through geographic licensing arrangements.

29 Pizzi R. Global Dialysis Industry Growing Despite Recession. Health Care Finance News, 2009.

The Company intends to take advantage of the customer access provided by Feraccru to raise awareness of PT20 and to leverage the commercial synergies that come with a common sales force.

5.5 Non-clinical and clinical research

The Group has conducted three material trials of PT20 since acquisition of the licence from the MRC; a non-clinical 28 day sub-chronic toxicity study in rats, a non-clinical 26 week chronic toxicity study, also in rats to investigate PT20 safety and iron deposition in order to support the clinical development programme, and a clinical Phase 2b pivotal study to evaluate the efficacy and safety of PT20.

The 28 day study provided supporting safety data for the application to conduct the Phase 2b pivotal study. The 26-week study provides support for Phase 3 development and the future NDA submission.

Phase 2b pivotal study

The Group conducted the Phase 2b pivotal study of PT20 in the US. This study completed in May 2015.

The study was a multicentre, double-blind, placebo controlled, randomised, multiple dose, Phase 2b pivotal study to evaluate the efficacy and safety of PT20 in CKD subjects with hyperphosphatemia who were dependent on dialysis. The primary objective of this study was to assess the effect of oral PT20 over placebo on phosphate levels after 28 days of dosing in subjects with dialysis dependent CKD.

In May 2015 positive results from the Phase 2b pivotal study were announced. PT20 met its primary endpoint ($p < 0.0001$) demonstrating that PT20 successfully lowered phosphate levels compared to placebo. All of the study's PT20 dose groups showed a phosphate reduction at day 28 compared to baseline and this reduction was dose related.

PT20 was very well tolerated with less than 5% of the patients who received study medication withdrawing because of adverse events and no serious Adverse Events were considered related to study medication. Some potentially positive haematological effects were noted and some iron absorption from PT20 was observed across all groups and this was consistent with prior data on PT20. Adverse Events were mostly GI in nature but generally uncommon and not dose related or dose-limiting.

The results from the Phase 2b pivotal study, together with the results of the non-clinical studies and other data, will assist the Group in finalising its plans for the Phase 3 programme and define the treatment regimen that will be taken forward into the Phase 3 study of PT20.

5.6 Future clinical research

A Phase 3 programme is required for regulatory approval to evaluate safety and efficacy and to assess PT20's ability to control phosphate levels in patients with hyperphosphatemia.

An IND has been opened for PT20 in the US, and a protocol for a Phase 3 CKD study design has been approved under this IND.

The data from these two pivotal studies are then expected to form the basis for new drug applications to the FDA and other health authorities for the approval of PT20 to control hyperphosphatemia, initially in patients dependent on dialysis.

5.7 Regulatory

PT20 is defined as a New Chemical Entity (''NCE''). Based on the package of data acquired from MRC, data subsequently developed by the Group and previous interactions MRC and the Group have had with the regulators, the Group is satisfied a clear pathway exists for regulatory approval of PT20 in both the US and EU markets.

Regulatory pathway

In the US the Group is considering utilising a 505b(2) regulation process. The Group intends to submit a non-clinical data package comprised of the Group's proprietary studies supplemented by reference to existing products containing ferric hydroxides. As PT20 is an NCE and the NDA approval will depend upon proprietary non-clinical and clinical data, the Group expects to benefit from full NCE data exclusivity provisions in the US.

In the EU, a standard route of regulatory approval will be followed for a NCE. In addition to the package submitted to the FDA, the Group anticipates that there may be the requirement to include additional non-clinical data.

Summary of past and planned interactions with regulators

The Company has not sought scientific advice from any European regulators at this stage. However, prior to receipt of the licence from the MRC, the MRC received scientific advice from the MHRA in January 2010. This advice reviewed the data available and the MHRA indicated that it is unlikely additional toxicology data would be required for PT20 and that the toxicology section of any Clinical Trial Application and future MAA may comprise of data for the individual components of PT20. In 2016, the Company expects to seek scientific advice from the EMA to confirm the details of the MAA pathway.

The Group obtained scientific advice (pre-IND meeting) from the FDA regarding the design of the Phase 2b and other aspects of the PT20 development plan. The FDA confirmed that the Phase 2b trial, if successful, could form one of the two pivotal studies required for approval.

The Group intends to seek further scientific advice from the FDA at an End of Phase 2 meeting in 2016 to discuss the design of the Phase 3 programme, and the data required to support an NDA.

Paediatric Plans

The Group is required to submit a paediatric development plan ("**PDP**") in the US within 6 weeks of the End of Phase 2 meeting. A paediatric development plan has not yet been developed. The Group proposes to submit a request for a deferral/partial waiver of paediatric studies before the New Drug Application ("NDA") is filed which, based on precedent, the Directors believe is likely to be granted.

5.8 Medical Affairs

Since acquisition of the licence from the MRC at the end of 2011, the Company has been consulting with a range of experts in the field and has conducted a number of formal meetings with these advisors to discuss and agree a suitable development programme for PT20. These include:

- PT20 kick-off meeting, Cambridge March 2012. This included advice from Geoffrey Block, MD and Dr Powell of the MRC to review and agree a strategy for the development of PT20.
- Scientific Advisory Board Meeting, Chicago May 2013. This meeting brought together 8 practising nephrologists from the US to discuss the outlook for PT20 and the proposed design of the Phase 2b pivotal study.
- Informal Advisory Board meeting, American Society of Nephrologists November 2014. Meeting with principal investigators and other KOLs in the sector to discuss PT20.

The Company intends to present the results of the Phase 2b pivotal study and to publish these results both as abstracts and in suitable peer reviewed journal(s).

- The first peer review publication is currently being drafted and the Company expects results to be published in 2016.
- The Phase 2b pivotal study results were presented at ASN in November 2015 with Dr Geoffrey Block the primary author. Further details of Dr Block are contained in the Key Advisors section of this Part 2 (*Information on the Company and the Group*) of this document.

5.9 Intellectual Property and MRC Licence

Pursuant to the MRC Licence, the MRC granted to PTL exclusive worldwide licences in respect of two key patent families and related know-how.

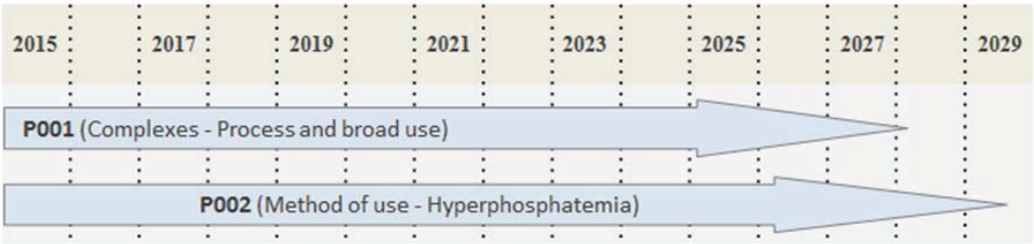
The patent families are:

- A platform patent covering technology relating to novel ligand modified poly oxo-hydroxy metal ion materials, termed Interstitial Mineral Hydroxides, their uses and processes for their preparation (PT20 patent family P001). This patent relates to a broad range of complexes and covers their production and use. It is exclusively licensed to PTL in the

relevant fields of phosphate binding for the treatment of renal diseases and/or intravenous iron for the treatment of IDAs. The patent family includes patents granted in the UK, Europe, the US and ten other territories worldwide, as well as patent applications pending in three territories.

- An application-specific patent relating to a ferric iron complex for use in the treatment of hyperphosphatemia (PT20 patent family P002). Given its specific application, this patent family is exclusively licensed to PTL. The patent family includes patents granted in the UK, the US and eight other territories, and patent applications pending in six territories, including Europe.

The chart below has been extracted from the Patent Agent's Report in Part 7 of this document. The chart summarises the terms of the key patent families for PT20 (except in the US where P001 expires in August 2029). Both patent families are partially granted, as explained above:



Under the terms of the MRC Licence, milestones of up to €9 million in aggregate remain payable upon the progression of PT20 into phase 3 clinical trials, upon first application for marketing authorisation in any jurisdiction and upon the grant of marketing authorisation in each of the EU, the US and Japan. In addition, high single-digit royalties are payable in respect of sales of PT20. PTL is also obliged to pay between 10 and 40% of any net licensing revenues for any sub-licences granted in relation to the licensed patent rights, depending upon the stage of development at which the sub-licence is granted.

PTL has agreed *inter alia* to use commercially reasonable endeavours to undertake the development and commercialisation of products covered by the licensed intellectual property, falling within the fields of phosphate binding for the treatment of renal diseases and intravenous iron for the treatment of IDA.

Under the terms of the MRC Licence, the MRC is primarily responsible for managing the filing, prosecution and maintenance of the patents licensed to PTL although it must consult with PTL (and PTL monitors the patents via its external patent attorneys). PTL pays 50 per cent. of the MRC's costs incurred in the filing, prosecution and maintenance of PT20 patent family P001 whilst PTL remains the only licensee (as the MRC is permitted to license this patent family outside of the fields of use relevant to PTL). PTL pays 100 per cent. of the MRC's costs incurred in the filing, prosecution and maintenance of PT20 patent family P002 (as this patent family is exclusively licensed to PTL without limitation as to field of use). MRC must inform PTL if it decides not to prosecute or maintain any of the applications or granted patents in either patent family and PTL may take over the prosecution/maintenance of such applications/patents (provided that if P001 has by then been licensed outside of the fields of use relevant to PTL, the best way forward in relation to that patent family must be discussed in good faith with the other licensee(s)).

The MRC has the right to terminate the MRC Licence if (i) PTL challenges the know-how or patents licensed by the MRC to PTL; (ii) PTL fails to remedy a material breach of the MRC Licence within 30 days of notice of the breach; or (iii) PTL suffers an insolvency event.

Unless terminated earlier, the MRC Licence continues until the later of (a) expiry of the relevant patent rights and (b) ten years after first commercial sale of a product.

Since the grant of the MRC Licence, significant investment has been made with regard to prosecuting the patents and patent applications. For further details regarding the patent families relating to PT20, including the current status of individual patents and patent applications, please refer to the Patent Agent's Report at Part 7 (*Patent Agent's Report*) of this document.

Trade marks

The Company does not currently have registered trade mark protection relating to PT20 given the earlier stage of the product compared to Feraccru. The Company will seek to obtain trade mark protection when and where appropriate.

Development Efforts

The Group has worked closely with the MRC in relation to the development of PT20 with the MRC undertaking chemical analysis work and assisting in the development of the manufacturing process as well as PT20 clinical trials designs. The MRC has also assisted PTL in its discussions with the relevant regulatory authorities in connection with PT20 clinical trials. All of this has helped to confirm the Directors' confidence in the quality of the design and delivery of the Group's clinical trials programmes and the execution of its business plan.

5.10 Manufacturing and supply

When PT20 was licensed from the MRC, the initial focus on activity was to begin the process of scale up from laboratory sized batches to full clinical trial manufacturing batches. This included the following key steps:

- Working with the MRC Laboratories in Cambridge to identify the key process steps and begin method transfer to the selected manufacturing partner;
- Selection of a suitable manufacturer of the Drug Substance;
- Selection of a suitable partner for the manufacture of the PT20 Drug Product; and
- Assay development work to develop a suitable set of methods to test the integrity and suitability of production batches.

Drug Substance

Drug Substance is manufactured under contract by Shasun Pharma Solutions (''Shasun'') in Dudley, Northumberland. Shasun is part of Shasun Pharmaceuticals Ltd, an Indian listed company with locations in the UK, India and the USA. Shasun and other vendors have been working closely with the Group since the PT20 licence was acquired to develop a scaled up manufacturing process suitable for supply of clinical trial supplies for the Phase 2b pivotal study and for the anticipated Phase 3 programme. This manufacturing process has developed from producing batches of less than 10g, to a completed phase 3 trial scale-up of up to 150kg batches. The drug substance has 24 months stability data.

Whilst the Group is satisfied with the capabilities of Shasun and its manufacturing process, the Directors are satisfied that this Drug Substance manufacturing process could readily be transferred to alternative Drug Substance producers if required.

Drug Product

The PT20 drug product used in the phase 2b study was a conventional pharmaceutical tablet containing either 400 mg or 800 mg iron oxide adipate (PT20). This formulation was developed by the Group together with its partners following the grant of the licence from the MRC. The product formulation used in earlier nutritional studies was a powder. Key progress since acquisition includes:

- 2012-13 Formulation Development – Produced a suitable 800 and 400mg tablet for Phase 2b pivotal study.
- 12 months stability data.

The drug product for the Phase 2 study was manufactured for the Group by Aesica Pharma in Nottingham. The Directors are satisfied that alternative manufacturers are available in Europe if required in the future.

5.11 Competition

As noted earlier, there are a number of products launched into the market. The competitive position varies significantly by geography:

- In the US, Renvela/Renagel is the largest with a share of approximately 80% based on reported US sales of €464m with the balance of market share from Shire's Fosrenol with approximately 10%. The newer iron based binders had a sub 5% share in 2014 as they had only just launched into the US market.
- In Europe, Renagel/Renvela reported sales in 2014 of €133m, representing 19% of Renagel/Renvela's total 2014 worldwide sales.
- In Japan, Fosrenol is the biggest selling product, marketed by Bayer Yakuhin Ltd. Total reported worldwide net sales in 2013 were £116.3m.

In addition, two iron (III)-based phosphate binders have been approved for marketing. Auryxia™ (Keryx), a ferric citrate compound, is approved in Japan under the name Riona® and was approved by the FDA in September 2014. Velphoro® (Vifor Fresenius), a ferric oxide-based treatment (sucroferric oxyhydroxide), was also approved by FDA in November 2013 and in the EU in June 2014.

A summary of the key competitors in the market is as follows:

Type	Product	Company	Generic name	Dosage	Daily pill burden
Calcium	Phoslo	Fresenius	Calcium acetate	Capsule	9 to 12
Calcium	Tums	GSK	Calcium carbonate	Chewable tablet	—
Resin	Renegel/ Renvela	Sanofi	Sevelemer carbonate	Tablet/Sachet	8 to 9
Heavy metal	Fosrenol	Shire	Lanthanum carbonate	Chewable tablet	3
Iron	Velphoro (US only)	Vifor Fresenius	Sucroferric oxyhydroxide	Chewable tablet	3
Iron	Auryxia (US) Fexeric (EU)	Keryx	Ferric citrate	Tablet	8 to 9

Key issues in the current competitive market include:

- The high pill burden inherent in current binders. This is due to their low specificity and the generally poor control of diet by patients failing to adhere to strict low-phosphate diets. Average pill loads for the current phosphate binders are in the range of 8-9 per day for the market leader (Renegel/Renvela) but many patients are at or above this. Although phosphate binders available as a chewable formulation have a lower pill load, they are extremely unpleasant to take.
- Current therapies for the treatment of hyperphosphatemia are less than satisfactory and Gfk's primary research indicated only a moderate degree of satisfaction with current treatment options.
- The high incidence of side effects. This goes hand in hand with high pill burden (which leads to high levels of drug being administered). Typical side effects include diarrhoea and other common GI effects.
- The current standard of care seeks to correct high serum phosphate levels to a level still above normal. The KDOQI guidelines from long term outcome studies suggest treating DD-CKD patients to control down to serum phosphate levels of <5.5 mg/dL. There is the potential to influence the guidelines and current treatment practice to seek to lower serum phosphate levels to normal levels. This would create significant additional demand for an effective phosphate binder.
- Price movement in the US market due to the threat of phosphate binders being included in the US renal ''bundle'' of capped service fees.

The potential introduction of generic competition. In 2014, and only in the US market, Impax laboratories agreed a deal with Sanofi for the latter to supply a branded generic version of sevelemer on a limited basis and in limited quantities. This was sold into the market at an approximately 10% discount to the prevailing Renegel/Renvela price. This was after the key patent expired in 2014. There are a number of other products where patent life is relatively short (Fosrenol to 2018 and Velphoro to 2016 for key US patents). It is likely therefore that generic versions of these products will eventually enter the market.

Phosphate binders in development

GfK have found there are relatively few late stage products in development for hyperphosphatemia.

6 Other Products

The Group is currently focused on the development of Feraccru and PT20 although the proceeds of the Placing receivable by the Company are intended to be applied substantially in relation to Feraccru. However, the Group does also have rights to other assets, which may be developed at an appropriate stage.

6.1 Sideromal

Sideromal is a nutritional supplement (ferrous maltol gluconate) which was manufactured prior to the Group's acquisition from Vitra Pharmaceuticals in 2010. It is a tablet containing 15 mg of elemental iron targeted at the treatment of mild IDA. The lower iron dosage and use of the recognised mineral ferrous gluconate as the starting material means that Sideromal is suitable to be marketed as a nutritional supplement under the EU classification system.

Historically, Sideromal was only sold to a small number of prescribers in the UK and no marketing support or activity was undertaken. Following its acquisition, for a transitional period, the Group initially permitted the continued supply of Sideromal to a limited number of patients in the UK, but it has now been entirely withdrawn from the market.

6.1.1 Sideromal Intellectual Property

Patents

The Sideromal product is protected by patent family P004, which comprises EP, US and Canadian granted patents. The patent term of this family continues until September 2021, except for the US patent which will expire in January 2022.

Trademarks

The product name SIDEROMAL is protected as a registered trade mark in the UK. The Group has also applied for trade mark protection for SIDEROMAL across the European Community. Further details are set out in the table below:

Trademark	Territory	Registration/ application no.	Status
SIDEROMAL	UK	2241570	Registered
SIDEROMAL	European Community	13779277	Pending

6.1.2 Sideromal future development opportunities

The Company could manufacture Sideromal to GMP standards with only limited manufacturing development required. Patented options for future exploitation of Sideromal include:

(a) Using Sideromal to develop an OTC/consumer brand as an iron supplement separate from Feraccru's market as a pharmaceutical product; and

(b) Out-licensing the technology to third parties.

The Company has no current plans to develop Sideromal.

6.2 PT30

The Company in conjunction with the MRC has conducted research to develop a novel IV iron product that aims to address the deficiencies of current IV iron products. This project has completed the initial product candidate identification phase, the next step being to expose these candidates to animals.

6.3 PT40

The company in conjunction with the MRC has conducted research into the development of a generic IV iron sucrose. The US dialysis market is potentially an attractive market with relatively near term potential given the shorter timescale and well-defined FDA-mandated pathway for regulatory approval of a generic IV iron product in the US. For example, sales of Galenica's IV Iron, Venofer, which is aimed directly at the dialysis market, were reported to be CHF 113.4 million in 2014.

After generation of promising preliminary data confirming proof of concept, the Company is planning a limited development once it has been able to obtain scientific advice from regulators in 2016. It may also initiate discussions with potential development partners.

The Directors believe that Sideromal, PT30 and PT40 have commercial potential to treat patients in areas of the market that Feraccru may not be able to address.

7 Commercial strategy

The commercial strategy of the Company has a number of key elements:

(a) To launch Feraccru into key European markets using its own field-based sales teams;

(b) To build a scalable central infrastructure to support this and future commercialisation efforts including elements such as business development and marketing;

(c) To ensure best use of clinical and pharmaco-economic data to develop the commercial arguments that will facilitate a premium price for Feraccru in its chosen markets yet ensure payers recognise the significant cost advantages of Feraccru over IV iron in the pricing achieved;

(d) To consider the plans for the launch of Feraccru into the US market, informed by the launch in Europe, either via out-licensing with a suitable partner or potentially using newly established field based teams and utilizing the established central infrastructure;

(e) To consider out-licensing PT20 to a commercial partner to conduct Phase 3 trials and to launch PT20 in certain markets with the Group potentially retaining the rights to core markets such as the EU, where the Company will be able to leverage its then existing commercial infrastructure;

(f) To consider, where appropriate, out-licensing opportunities for Feraccru in peripheral markets, in-licensing or acquiring other products whether already marketed or close to market that would enhance the Company's offering in its core markets, particularly focused on products that bolt onto the core iron deficiency offering with Feraccru and enhance the indication specialisms;

(g) To seek to change the treatment guidelines for the treatment of IDA in general and specifically in core indications such as IBD and CKD to have Feraccru recognised as clear second line therapy ahead of IV iron; and

(h) To consider further development or out-licence opportunities for other assets including PT40.

Structure of the commercial organisation

The design of the Company's commercial stage structure is based on a core central team that provides scientific, development, commercialisation and marketing leadership, the implementation of which will be devolved to local operations in key territories which will each have a dedicated clinical and medical team with appropriate support to drive commercial uptake of the Company's products.

Expansion opportunities

The Company is currently focused on commercialising Feraccru and completing the clinical development of PT20 ahead of commercialisation. While there are no current plans, the Company would give due consideration to commercially compelling opportunities that would enhance or strengthen its offering, including licensing or acquiring complimentary products or technologies.

8 Regulatory overview

On 17 December 2015 the CHMP unanimously adopted a positive opinion that Feraccru be granted a marketing authorisation in all member states of the European Union. This marketing authorisation is scheduled to be issued in the first quarter of 2016. Following the grant of the marketing authorisation in the EU, the Company will also focus on obtaining US approval and EU indication extension. A Phase 3 CKD protocol design has already been accepted by FDA under the US IND.

Furthermore a clear pathway to regulatory approval has been agreed with FDA for PT20 and additional scientific advice will be sought from the EU CHMP in 2016. A dialogue has been opened with the FDA in order to agree the quality data package that will be included in an ANDA for generic iron sucrose (PT40).

Data and marketing exclusivity in the European Union

8.1 In the European Union, the first applicant for approval of a new medicinal product developed independently to existing products is protected by ten years of data and marketing exclusivity from the date of grant of the marketing authorisation. An additional year may be obtained in a number of circumstances, such as where the innovator company is granted a marketing authorisation for a significant new indication for the relevant medicinal product. This protection period runs concurrently with any remaining patent term for the product meaning that data exclusivity provides additional protection to the innovator when the remaining patent length is shorter than the data exclusivity period at the time of approval or to the extent that the patent term is circumvented by a generic product prior to its expiry.

Regulatory approval (marketing authorisation) process

8.2 Prior to marketing a medicinal product, a marketing authorisation must be obtained. Governmental authorities in the US, the European Union and most other jurisdictions where the Company intends to distribute its products regulate, among other things, the research, development, clinical testing, manufacture, approval, distribution, marketing and monitoring and reporting of pharmaceutical products. Obtaining regulatory approvals and ensuring subsequent compliance with applicable laws and regulations can be a lengthy process involving substantial financial and managerial resources. Regulatory requirements vary from jurisdiction to jurisdiction, and the timing and success of efforts to obtain regulatory approvals can be highly uncertain.

Non-clinical testing

8.3 Non-clinical testing generally includes an evaluation of a product's safety profile through laboratory and animal testing. The primary purpose of non-clinical work is to develop detailed information to support a decision that it is reasonably safe to proceed with human studies of the product in addition to support commercial availability.

Clinical studies

8.4 Clinical studies generally involve the administration of the product to human patients to evaluate its safety, tolerability, efficacy and dosage. Phase 1 studies are primarily to assess safety rather than efficacy.

8.5 In a phase 2 study, a new product is studied in trials to identify possible adverse effects and safety risks, and to explore the preliminary or potential efficacy of the product, as well as dosage tolerance and the optimal effective dose. Phase 2 studies are sometimes further divided into two phases: phase 2a trials are designed to assess dosage range (how much product subjects should be given); and phase 2b trials are specifically designed to study definite dose range and efficacy (how well the product works at a prescribed dose). Some

phase 2 trials may be designed as randomised clinical studies, where some subjects receive the product and others receive a placebo/standard treatment. Randomised phase 2 trials typically have fewer subjects than randomised Phase 3 trials.

8.6 When phase 2 trials demonstrate that a specific dosage range of the product is likely to be effective and has an acceptable safety profile, confirmatory phase 3 trials are undertaken. The phase 3 studies are intended to provide an adequate basis for establishing the benefit/risk ratio for a subsequent application for marketing approval. Therefore, a sufficiently high number of subjects must be enrolled and exposed to the product for a duration which will provide adequate efficacy and safety data for the envisaged clinical use. The studies are usually controlled, i.e. compare the product to placebo and/or to active treatment depending on the medical condition and the product under investigation. As a result of their size and duration, phase 3 trials are the most expensive to design and run.

Regulatory approval

Regulation in the US

8.7 In the US, the FDA specifies requirements covering the testing, safety, effectiveness, manufacturing, labelling, approval and marketing of prescription pharmaceuticals, pursuant to the Food, Drug and Cosmetic Act 1938 and its implementing regulations. Following non-clinical tests and before starting human clinical studies, a company must submit an Investigational New Drug application to the FDA.

8.8 Assuming successful completion of the required clinical testing, the results of the non-clinical testing and clinical studies, together with other detailed CMC information, are submitted to the FDA in the form of an NDA, requesting approval to market the product. The FDA reviews an NDA to determine, among other things, whether a product is safe and effective for its intended use. Before approving an NDA, the FDA may also inspect the facility or facilities where the product is manufactured and/or the pivotal clinical trial sites.

8.9 Following approval by the FDA, a post-marketing monitoring stage may be required, during which safety updates are required to be submitted to the FDA. They include reports of adverse events, as well as any new study results that are available whether published or not (including those published in other countries). The FDA also receives Adverse Event reports directly from healthcare providers, manufacturers and patients during this period. The FDA reviews and analyses the reports to assess the frequency and seriousness of the Adverse Events, and evaluates the aggregate public health benefit of the product compared to its evolving risk profile. Failure to comply with post-marketing regulatory requirements can result in the suspension of a regulatory approval, as well as in civil and criminal sanctions.

Regulation in Europe

8.10 To be permitted to market a pharmaceutical product in more than one country in Europe, pharmaceutical companies can submit a single marketing-authorisation application (MAA) to the EMA. Once granted by the European Commission, a centralised marketing authorisation is valid in all EU Member States, as well as in the European Economic Area countries Iceland, Liechtenstein and Norway. The Committee for Human Medicinal Products is the scientific committee of the EMA that is responsible for the scientific evaluation of centralised MAA applications on behalf of the European Commission. The Commission marketing approval (''Decision'') is based on the scientific ''Opinion'' adopted by the CHMP.

8.11 Assuming successful completion of the required clinical testing, the results of the non-clinical and clinical studies, together with other detailed CMC information, are submitted to the EMA. Following this application, a scientific evaluation is carried out through the EMA's Committee for Medicinal Products for Human Use. Each Member State has one representative in the CHMP. If the CHMP concludes that the quality, safety and efficacy of the medicinal product are sufficiently proven, it adopts a positive opinion using a qualified majority voting system. This is sent to the European Commission, which may grant a single marketing authorisation that allows the product to be put on the market in all Member States.

8.12 Failure to comply with post-marketing regulatory pharmaco-vigilance requirements can result in the suspension of a regulatory approval, as well as in civil and criminal sanctions. The EMA also receives reports from healthcare professionals and patients of suspected side effects of authorised products. This additional monitoring scheme applies to products for which there is relatively little information available compared to other existing products.

PART 3

RISK FACTORS

In addition to all other information set out in this document, the following specific risk factors should be considered carefully by potential investors in evaluating whether to make an investment in the Company. The investment described in this document may not be suitable for all those who receive it. Before making a final decision, investors who are in any doubt are advised to consult their stockbroker, bank manager, solicitor or accountant or other independent professional adviser authorised under the FSMA who specialises in advising on the acquisition of shares and other securities in the United Kingdom.

You should carefully consider the risks described below and ensure that you have read this document in its entirety before making a decision to invest in the Company.

Any investment in the Ordinary Shares and Warrants is subject to a number of risks. Prospective investors should consider carefully the factors and risks associated with any such investment in the Ordinary Shares and Warrants, the Company's business and the industry in which it operates, together with all of the information set out in this document including, in particular, the risks described below.

There can be no certainty that the Company will be able to implement successfully the strategy set out in this document. No representation is or can be made as to the future performance of the Company and there can be no assurance that the Company will achieve its objectives.

The Directors believe that the risks described below are the material risks relating to the Ordinary Shares and Warrants at the date of this document. The following is not an exhaustive list or explanation of all risks that prospective investors may face when making an investment in the Ordinary Shares and Warrants and should be used as guidance only. Additional risks and uncertainties not currently known to the Directors, or that the Directors deem immaterial at the date of this document, may also have an adverse effect on the Company's business, prospects, results of operations and financial condition and, if any such risk should occur, the price of the Ordinary Shares and Warrants may decline and prospective investors could lose all or part of their investment.

If any events or circumstances giving rise to any of the following risks, together with possible additional risks and uncertainties of which the Company and the Directors are currently unaware or which the Company and the Directors consider not to be material in relation to the Company's business, actually occur, the Company's business, financial condition and results of future operations could be materially and adversely affected. In such circumstances, the value of the Ordinary Shares and Warrants could decline due to any of these risks occurring and investors could lose part or all of their investment. In particular, the Company's performance may be affected by changes in market or economic conditions and in legal, regulatory and tax requirements.

Prospective investors should consider carefully whether an investment in the Ordinary Shares and Warrants is suitable for them in the light of the information in this document and their personal circumstances.

1 Risks relating to the Company's business, financial position and to the development and regulatory approval of its products.

1.1 The development of pharmaceutical products is inherently uncertain and has high failure rates, even in late-stage product development programmes.

The Company's two lead products are in different phases of clinical development. There is a high failure rate in the development of pharmaceutical products and there is a substantial risk of adverse, undesirable, unintended or inconclusive results from testing or clinical trials, which may substantially delay, or halt entirely, or make uneconomic, any further development of the Company's products and may prevent or limit the commercial use of such products. Whilst the pivotal Phase 3 Study data has been generated in IDA in IBD, the Group is currently conducting a Phase 3b study comparing Feraccru with IV iron. In addition, management also intends to conduct Phase 3 trials in patients who have CKD and IDA and in paediatrics who suffer from IDA. Due to these inherent risks involved in developing pharmaceutical products, there is a risk some of the Company's products will not ultimately be successfully developed or launched.

In addition, later phase clinical trials of PT20 may fail to show the desired safety and efficacy, despite it having progressed through early phase clinical trials. Successful completion of one stage of development of a pharmaceutical product does not ensure that subsequent stages of development will be successful.

The inability of the Company to market any of its products currently under development would adversely affect the Company's business and financial condition.

The Company intends to conduct additional trials and undertake further development work on Feraccru after it receives its first marketing authorisations to provide additional data for marketing purposes or to permit wider label claims. If such additional testing is not completed on time or within budget, does not deliver the expected improvement in commercial potential or identifies issues which adversely affect Feraccru, it could materially and adversely affect the Company's business, financial condition, results of operations and prospects.

1.2 The Group is dependent primarily on Feraccru for its short and medium term success.

The Group is dependent on one principal product for its short and medium term success: Feraccru. Feraccru has completed a Phase 3 clinical study in Europe and is planning a Phase 3 study in the US. The Group submitted its MAA to EMA in December 2014 and received a unanimous positive CHMP recommendation in December 2015. It plans to seek marketing approval in the US once the US Phase 3 trial is complete. In particular, the Directors anticipate receiving EU marketing authorisation for Feraccru in the first quarter of 2016. If that approval is delayed or not received at all, there would be a material adverse effect on the Group's business and prospects.

Any unexpected other negative development with respect to Feraccru (for example, delays in receipt of, or failure to receive, other regulatory approvals, unexpected safety or efficacy concerns, manufacturing or supply delays) may have a material adverse effect on the financial condition and prospects of the Group.

The success of Feraccru will depend on a number of factors, including:

(a) receipt of marketing approvals for Feraccru in the United States and other jurisdictions where separate approval is required and where the Company subsequently chooses to market Feraccru;

(b) launching commercial sales of Feraccru, if and when approved;

(c) acceptance of Feraccru by patients, the medical community and third-party payers;

(d) Feraccru competing effectively with existing therapies and in particular with intravenous products addressing the same clinical needs;

(e) Feraccru influencing the treatment guidelines in relevant territories;

(f) Further clinical trials to provide additional data to support commercialisation of Feraccru and to permit wider label claims; and

(g) risk of lower adherence to Feraccru as an oral therapy compared to current IV products typically administered in a hospital setting.

1.3 Even if the Company receives regulatory approval for Feraccru, PT20 or any other products, it may be unable to commercialise them.

The Company is preparing to commercially launch Feraccru across major European markets and will therefore have to develop its own infrastructure in these territories, including sales and marketing functions but these functions are not yet fully developed. Although the Company has in place commercial distribution rights to certain territories that it considers to be non-core, to achieve commercial success for any approved product, the Company must develop or acquire a sales and marketing function, outsource these functions to third parties or enter into partnerships.

There are a number of factors that may inhibit the Company's efforts to commercialise Feraccru on its own including:

(a) the Company's inability to recruit, train and retain adequate numbers of effective sales and marketing personnel;

(b) the inability of sales personnel to obtain access to or persuade adequate numbers of potential practitioners to prescribe any future products;

(c) unforeseen costs and expenses associated with creating an independent sales and marketing organisation;

(d) costs of marketing and promotion above those anticipated by the Company; and

(e) inability to secure a suitable level of pricing and/or reimbursement approval from the relevant regulatory authorities in the countries it is targeting.

Whilst the Company is only seeking to enter into arrangements with third parties to perform sales and marketing services in non-core territories, any such arrangements could result in the Company's product revenues (or the profitability of such product revenues to the Company) being lower than if the Company were to market and sell the products itself. In addition, the Company may not be successful in entering into arrangements with third parties to sell and market its products or may be unable to do so on terms that are favourable to the Company. Acceptable third parties may fail to devote the necessary resources and attention to sell and market the Company's products effectively.

If the Company does not establish sales and marketing capabilities successfully, either on its own or in collaboration with third parties, it will not be successful in commercialising its products, which in turn would have a material adverse effect on its business, prospects, financial condition and results of operations.

The Company has also invested and will continue to invest resources into the development of other products, including PT20. Even where these products are successfully developed and marketing approval is secured from relevant regulatory authorities, these products might not achieve commercial success.

Factors which could limit commercial success of a product include but are not limited to:

(a) limited market acceptance or a lack of recognition of the unmet medical need for the product amongst prescribers;

(b) new competitor products entering the market;

(c) the number and relative efficacy, safety or cost of competitive products;

(d) an inability to supply a sufficient amount of the product to meet market demand;

(e) insufficient funding being available to market the product adequately;

(f) an inability to enforce intellectual property rights, or the existence of third party intellectual property rights;

(g) safety concerns arising pre or post-launch resulting in negative publicity or product withdrawal or narrowing of the product label and the group of persons who may receive the product;

(h) labelling being restricted/narrowed in the future and in the future by regulatory agencies; and

(i) refusals by government or other healthcare payors to fund the purchase of the products by healthcare providers at a commercially viable level (or at all) or otherwise to restrict the availability of approved products on other grounds.

If any of the foregoing were to occur, it could materially and adversely affect the Group's business, financial condition and results of operations and prospects.

1.4 If sufficient revenue is not generated from operations or the Warrants are not exercised in full, additional financing may be required which may not be available at all or, if available, may be on terms which dilute Shareholders' interests.

The Company expects to incur further significant expenses in connection with its ongoing commercialisation and research and development activities in relation to its products, including for funding clinical studies, registration, manufacturing, marketing, sales and distribution. In order to finance fully the Company's business plan set out in Part 2 (*Information on the Company and the Group*) of this document, the Company may require more capital than is available from its existing cash balances and the net proceeds of the Placing. In the event that all the Warrants are exercised, the Directors expect to receive approximately £17.5 million of additional funds that, together with the Company's existing cash balance and the proceeds

from the Placing, will be used to finance the business plan. However, warrantholders are under no obligation to exercise their Warrants and, if they fail to do so, the Company will not receive any funding pursuant to the Warrants.

In addition, whilst the Company is expecting to generate first revenues from product sales in 2016, it does not envisage being self-sustaining for a period of time after that and there is no certainty those revenues will materialise. The Company may therefore need to obtain additional funding (for the avoidance of doubt, not during a period at least 12 months from the date of this document) before it becomes self-sustaining.

Access to adequate additional financing, whether through debt financing, an equity capital raise or a suitable out-licensing or partnering transaction may not be available to the Company on acceptable terms, or at all. If the Company is unable to raise capital, the Company could be forced to delay, reduce or eliminate its research and development programmes or commercialisation efforts. Any additional equity fundraising may be dilutive for Shareholders.

Any of these events could have a material adverse effect on the Company's development, growth, financial condition and prospects and may lead the Company to delay, reduce or abandon research and development programmes or commercialisation of some of its products.

1.5 If the Company obtains regulatory approval for a product, the product will remain subject to ongoing regulatory obligations.

If the Company obtains regulatory approval in a jurisdiction, regulatory authorities may still impose significant restrictions on the indicated uses or marketing of the product, or impose ongoing requirements for potentially costly post-approval studies or post-market surveillance.

In addition, product manufacturers and their facilities are subject to continual review and periodic inspections by the EMA, the FDA and other regulatory authorities for compliance with good manufacturing practices and good pharmacovigilance practices. If the Company or a regulatory agency discovers previously unknown problems with a product or problems with the facility where the product is manufactured, a regulatory agency may impose restrictions relative to that product or the manufacturing facility, including requiring recall or withdrawal of the product from the market or suspension of manufacturing.

If the Company fails to comply with applicable regulatory requirements following approval of any of the products, a regulatory agency may:

(a) issue a warning letter asserting that the Company is in violation of relevant laws;

(b) seek an injunction or impose civil or criminal penalties or monetary fines;

(c) suspend or withdraw regulatory approval;

(d) suspend any ongoing clinical studies;

(e) seize the product; or

(f) refuse to allow the Company to enter into supply contracts, including government contracts.

Any governmental investigation of alleged violations of law could require the Company to expend significant time and resources and could generate negative publicity. The occurrence of any event or penalty described above may delay commercialisation of the Company's products, increase costs and materially and adversely affect the Company's business, results of operations or financial condition.

1.6 Insurance coverage and reimbursement may be limited, unavailable or may be reduced over time in certain market segments for the Company's products.

Government authorities and third-party payers, such as private health insurers, decide which pharmaceutical products they will cover and the amount of reimbursement. Reimbursement may depend upon a number of factors, including the payer's determination that use of a product is: (i) safe, effective and medically necessary; (ii) appropriate for the specific patient; and (iii) cost-effective.

Obtaining coverage and reimbursement approval for a product from a government or other third-party payer is a time-consuming and costly process that could require the Company to provide supporting scientific, clinical and cost-effectiveness data for the use of its products. The Company may not be able to provide data sufficient to gain acceptance with respect to coverage and reimbursement, or to demonstrate commercial value compared to, in the case of Feraccru, IV products or the risk of comparison with OFP's. If reimbursement of the Company's products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, the Company may be unable to achieve or sustain profitability.

The Company intends to seek approval to market its products in the EU, the United States and in selected other jurisdictions with the initial focus for Feraccru being the EU. In the EU, the pricing of prescription pharmaceuticals is subject to national governmental control and pricing negotiations with governmental authorities can, in some circumstances, take several years after obtaining marketing approval for a product. In addition, market acceptance and sales of the Company's products will depend significantly on the availability of adequate coverage and reimbursement from third-party payers and may be affected by existing and future health care reform measures.

The continuing efforts of governments, insurance companies, managed care organisations and other payers of healthcare services to contain or reduce costs of healthcare and/or impose price controls may adversely affect the Company's ability to set prices for its products, generate revenues and achieve or maintain profitability. Any reduction in government reimbursement programmes may result in a similar reduction in payments from private payers, which may adversely affect the Company's business, prospects, financial condition and results of operations.

1.7 The clinical trials process is expensive and time consuming

The Group is currently conducting a Phase 3b study comparing Feraccru with IV iron. In addition, management also intends to conduct Phase 3 trials in patients who have CKD and IDA and in paediatrics who suffer from IDA.

Many countries, including all members of the EU, the US and Japan, have very high standards of technical appraisal for prescription pharmaceutical products and, accordingly, the clinical trial process is, in most cases, lengthy and therefore expensive. Clinical trials need to be correctly designed to satisfy regulators, investigators, hospital ethics committees, customers and distributors, which can be time-consuming and expensive, and it is not always possible quickly and efficiently to identify a sufficient number of patients who meet the trial criteria. If the cost and timing of the Company's planned clinical and non-clinical trials exceeds the Directors' current expectations, this could significantly impact the Company's development plan for that product.

Delays in obtaining the necessary regulatory approvals for products to be sold by the Group may result in the emergence of competing products and/or the loss of life span of granted patents or data exclusivity protecting the Group's products from competition, may materially reduce the Group's potential future revenues and profitability.

The successful completion of the development of a product does not necessarily mean that it will ultimately be approved or that such approval will be maintained following the commercial launch of the product.

1.8 If the Company experiences delays or difficulties in the enrolment of subjects in clinical studies, its receipt of necessary regulatory approvals could be delayed or prevented.

Whilst further studies are not required in respect of its centralised application for regulatory approval by the EMA for Feraccru, the Directors intend to conduct additional Phase 3 studies in order to expand the target market beyond patients who suffer from IDA with IBD. It may not be able to initiate or continue additional clinical studies for its products if it is unable to locate and enrol a sufficient number of eligible subjects to participate in these studies as required by applicable regulatory authorities.

In addition, some of the Company's competitors may have ongoing clinical studies for products that treat the same indications as the Company's products, and subjects who would otherwise be eligible for its clinical studies may instead enrol in clinical studies of its competitors' products.

Subject enrolment is affected by other factors including:

(a) the severity of the indication under investigation;

(b) the subject eligibility criteria for the study in question;

(c) the perceived risks and benefits of the product under the study;

(d) the Company's payments to participants and third-parties for conducting clinical studies;

(e) the referral practices of physicians;

(f) the ability to monitor subjects adequately during and after treatment; and

(g) the proximity and availability of clinical study sites for prospective subjects.

Any difficulties in enrolling a sufficient number of subjects for any of its clinical trials could result in significant delays and could require the Company to abandon one or more clinical trials altogether. Enrolment delays in the Company's clinical studies may result in increased development costs for its products and in delays to commercially launching its products, if approved. If any of these factors materialise, the Company's business, results of operations or financial condition could be materially adversely affected.

1.9 The Company operates in a highly regulated environment

The Company operates in a highly regulated environment. During the period before any of its products are approved for commercial sale, the Company and its approved partners must operate to relevant standards of conduct including GCP and GMP and follow relevant ICH guidelines in the conduct of any clinical studies. Whilst the Company maintains and operates suitable quality standards and practices including the audit of key suppliers, there is a risk that an inspection by a relevant regulatory authority may result in adverse findings that inhibit the Group's ability to conduct its research and development activity.

In respect of products marketed once regulatory approval has been obtained, the Company is required to adhere to relevant quality requirements including the maintenance of appropriate and adequate pharmaco-vigilance systems for monitoring adverse events and other quality and safety issues in territories in which its products are marketed. There is a risk that such a system is not deemed to be adequate or appropriate by a relevant regulatory authority and that would have a negative impact on its ability to market its products in such territories.

In addition, as is the case with all registered pharmaceutical products, the Company will be required to monitor the safety of its products once they are being prescribed in territories for which it has approval to market its products. Whilst the Company has acquired, referenced and generated a wide body of positive evidence in respect of the safety profile of both Feraccru and PT20, there is a risk that either its monitoring framework is not adequate or that data emerges on any of its marketed products that leads to safety concerns or issues and negatively impacts the ability of the Company to continue to market its products.

1.10 Changes in the regulatory environment could result in delays or failures by the Company to manufacture or sell products.

The Company may experience delays or rejections based upon additional government regulation from future legislation or administrative action, or changes in regulatory agency policy during the period of product development, clinical studies and the review process. Regulatory agencies also may approve a treatment candidate for fewer or more limited indications than requested or may grant approval subject to the performance of post-marketing studies. In addition, regulatory agencies may not approve the labelling claims that are necessary or desirable for the successful commercialisation of the Company's products. Any of these actions could have a material adverse effect on the business or prospects of the Company. The Company consults with several regulatory agencies including FDA, EMA and other national European agencies and is not aware of any relevant proposed changes in the regulatory environment.

1.11 The SHG Group and PTL have incurred significant losses since the Group's inception and the Directors anticipate that the Group will continue to incur significant losses for the foreseeable future.

The amount of the Company's future net losses will depend, in part, on the rate of its future expenditures including further research and development activity. The amount of net losses will also depend on the Company's success in developing and commercialising Feraccru and other products that generate significant revenue. Any failure by the Company to become and remain profitable could depress the value of the Ordinary Shares and Warrants and could impair its ability to expand its business, maintain its research and development efforts, diversify its product offerings or continue its operations.

1.12 The Company's limited operating history may make it difficult for a prospective investor to evaluate the success of the Company's business to date and to assess its future viability.

The Group was founded in 2008. To date, its activities have been limited to business planning, fundraisings, acquiring and developing its products, undertaking clinical trials and applying for regulatory approvals. No regulatory approvals have yet been obtained and the Company has not yet demonstrated its ability to conduct sales and marketing activities necessary for successful product commercialisation. The Company may not be successful in these new areas and any such failure would materially and adversely affect the Company's business, results of operations and financial position.

1.13 The Company faces significant competition from other pharmaceutical companies.

The Company has competitors internationally, including major multinational pharmaceutical companies, universities and other research institutions.

In respect of Feraccru, there are a number of established companies engaged in the development and marketing of intravenous iron-based preparations addressing the Iron Deficiency Anaemia market and in particular in patients who have previously failed treatment on Oral Ferrous Products. In addition, there are a wide range of OFPs addressing the IDA market currently approved and marketed by a number of large and small pharmaceutical companies.

In respect of PT20, there are a number of current marketed products seeking to address the market for hyperphosphatemia and a number of products in development. There is a risk that there may be little to differentiate PT20 from other phosphate binders. If this is the case, then there is a risk that price will play a role in influencing uptake of PT20. Certain competitor products have reached or are due to reach in the foreseeable future the end of patent life and therefore new generic competition is anticipated in this market, particularly in the US. Whilst such changes to the competitive landscape have been considered in the Company's plans in respect of the planned development of PT20, there is a risk that such competition adversely impacts the ability for the Company to market PT20 successfully in its planned markets.

Many of its competitors have substantially greater financial, technical and other resources, such as a larger research and development team and proven marketing and manufacturing organisations and well-established sales forces. The Company's competitors may succeed in developing, acquiring or licensing, drug products that are more effective or less costly than products which the Company is currently developing or which it may develop.

Established pharmaceutical companies may invest heavily to accelerate the discovery and development of products that could make the Company's products less competitive. In addition, any new product that competes with an approved product must demonstrate compelling advantages in efficacy, convenience, tolerability or safety in order to overcome price competition and to be commercially successful. Accordingly, its competitors may succeed in obtaining patent protection, receiving FDA and EMA approval or discovering, developing and commercialising pharmaceutical products before the Company does, which would have a material adverse impact on the Company's business.

The availability and price of the Company's competitors' products could limit the demand, and the price the Company is able to charge, for any of its products, if approved for sale. The Company will not achieve its business plan if acceptance is inhibited by price competition or the reluctance of physicians to switch from existing drug products to the Company's products

or if physicians switch to other new drug products or choose to reserve its products for use in limited circumstances. Competition from lower-cost generic pharmaceuticals may also result in significant reductions in sales volumes or sales prices for the Company's products, which could materially adversely affect its business, prospects, financial condition and results of operations.

2 The Company is dependent on third party supply, development and manufacturing and clinical service relationships and on single manufacturing sites for certain products

The Company's business strategy utilises the expertise and resources of third parties in a number of areas including the conduct of clinical trials, other product development, manufacture and the protection of the Group's intellectual property rights in various geographical locations. This strategy creates risks for the Company by placing critical aspects of the Company's business in the hands of third parties whom the Company may not be able to manage or control adequately and who may not always act in the best interests of the Company.

Where the Company is dependent upon third parties for the development or manufacture of certain products, the Company's ability to procure their development or manufacture in a manner which complies with regulatory requirements may be constrained, and its ability to develop and deliver such material on a timely and competitive basis may be adversely affected, which may impact revenues.

The Group is also currently reliant on Piramal for the manufacture of Feraccru. There may be disruptions in supplies, including delays due to the inability of the Company's manufacturers to supply products on a timely basis. In addition, ongoing discussions with a number of alternative suppliers aiming to reduce reliance on Piramal could prove to be unsuccessful.

Regulatory requirements for pharmaceutical products tend to make the substitution of suppliers and contractors costly and time-consuming. Alternative suppliers may not be able to manufacture products effectively or obtain the necessary manufacturing licences from applicable regulatory authorities. The unavailability of adequate commercial quantities, the inability to develop alternative sources, a reduction or interruption in supply of contracted services, or a significant increase in the price of materials and services, could have a material adverse effect on the Company's ability to manufacture and market its products or to fulfil orders from its distributors or licensees, which in turn would have an adverse impact on its cash flows.

3 Risks relating to the Company's Intellectual Property

3.1 The expiry of certain intellectual property rights or an inability to obtain, maintain or enforce adequate intellectual property rights for products that are marketed or in development may result in additional competition from other third party products. Third parties may have blocking intellectual property rights which could prevent the sale of products by the Group or require that compensation be paid to such third parties.

The extent of the Group's success will, to a significant degree, depend on its ability to establish, maintain, defend and enforce adequate intellectual property rights and to operate without infringing the proprietary or intellectual property rights of third parties. The Group has been granted, or has in-licensed rights under, a number of key patent families for Feraccru and PT20 (or other proprietary rights), and patent applications are pending in the United States, Europe, and certain other jurisdictions. The Group might develop or acquire further technology or products that are not patentable or otherwise protectable. The strength of patents in the pharmaceutical field involves complex legal and scientific questions and can be uncertain. Patents or other rights might not be granted under any pending or future applications filed or in-licensed by the Group and any claims allowed might not be sufficiently broad to protect the Group's technologies and products from competition. Competitors may also successfully design around key patents held by the Group, thereby avoiding a claim of infringement. There is a risk that not all relevant prior art has been identified with respect to any particular patent or patent application and the existence of such prior art may invalidate any patents granted (or result in a patent application not proceeding to grant). Patents or other registerable rights might also be revoked for other reasons after grant. Third parties may challenge the validity, enforceability or scope of any granted patents. The Group's

defence of its proprietary rights could involve substantial costs (even if successful) and could result in declarations of invalidity or significantly narrow the scope of those rights, limiting their value.

Competitors may have filed applications or been granted patents, or obtained additional patents and proprietary rights, that relate to and could be infringed by the Group's products. An adverse outcome with respect to third party rights such as claims of infringement of patents or third-party proprietary rights by the Group could subject the Group to significant liabilities or require the Group to obtain a licence for the continued use of the affected rights, which may not be available on acceptable terms or at all, or require the Group to cease commercialisation and development efforts, or the sale of the relevant products, in whole or in part in the relevant jurisdictions.

The Group could be subject to claims for compensation by third parties claiming an ownership interest in the intellectual property rights relating to a commercially successful product. This may include claims from employee inventors in territories which permit such claims even where the Group owns the intellectual property rights in question.

Any such failure to defend the Group's proprietary intellectual property could have a material adverse effect on the Group's business, prospects, financial condition and results of operations.

3.2 The Company may not be able to obtain, maintain, defend or enforce the intellectual property rights covering its products.

To date, the Company has had certain patents granted to it in jurisdictions it considers to be important to its business. However, the Company cannot predict:

(a) the degree and range of protection any patents will afford against competitors and competing technologies, including whether third parties will find ways to invalidate or otherwise circumvent the patents by developing a competitive product that falls outside its scope;

(b) if, when and where additional patents will be granted;

(c) that granted patents will not be contested, invalidated or found unenforceable;

(d) whether or not others will obtain patents claiming aspects similar to those covered by the Company's patents and patent applications;

(e) whether the Company will need to initiate litigation or administrative proceedings, or whether such litigation or proceedings will be initiated by third parties against the Company, which may be costly and time consuming; and

(f) whether third parties will claim that the Company's technology infringes upon their rights.

Patent protection is of importance to the Company in maintaining its competitive position in its planned product lines and a failure to obtain or retain adequate protection could have a material adverse effect on the Company's business, prospects, financial condition and results of operations.

3.3 The Company may not be able to prevent disclosure of its trade secrets, know-how or other proprietary information (''Confidential Information'').

The Company relies on trade secret protection to protect its interests in proprietary know-how and in processes for which patents are difficult to obtain or enforce. If the Company is unable to protect its trade secrets adequately the value of its technology and products could be significantly diminished. Furthermore, the Company's employees, consultants, contract personnel or third-party partners, either accidentally or through wilful misconduct, may cause serious damage to its programmes and/or its strategy by disclosing Confidential Information to third parties. It is also possible that Confidential Information could be obtained by third parties as a result of breaches of the Company's physical or electronic security systems. Any disclosure of confidential data into the public domain or to third parties could allow the third parties to access Confidential Information and use it in competition with the Company. In addition, others may independently discover the Company's Confidential Information. Any action to enforce the Company's rights against any misappropriation or unauthorised use and/or disclosure of Confidential Information is likely to be time-consuming and expensive, and may ultimately be unsuccessful, or may result in a remedy that is not commercially valuable.

3.4 The Company's products could infringe patents and other intellectual property rights of third parties.

The Company's commercial success depends upon its ability, and the ability of any third party with which it may partner to develop, manufacture, market and sell its products and use its patent-protected technologies without infringing the patents of third parties.

The Company's products may infringe or may be alleged to infringe existing patents or patents that may be granted in the future which may result in costly litigation and could result in the Company having to pay substantial damages or limit the Company's ability to commercialise its products.

Because some patent applications in Europe and the United States may be maintained in secrecy until the patents are issued, patent applications in Europe, the United States and many foreign jurisdictions are typically not published until 18 months after filing, and publications in the scientific literature often lag behind actual discoveries, the Company cannot be certain that others have not filed patents that may cover its technologies, its products or the use of its products. Additionally, pending patent applications which have been published can, subject to certain limitations, be later amended in a manner that could cover the Company's technologies, its products or the use of its products. As a result, the Company may become party to, or threatened with, future adversarial proceedings or litigation regarding patents with respect to its products and technology.

If the Company is sued for patent infringement, the Company would need to demonstrate that its products or methods either do not infringe the patent claims of the relevant patent or that the patent claims are invalid, and the Company may not be able to do this. If the Company is found to infringe a third party's patent, the Company could be required to obtain a licence from such third party to continue developing and marketing its products and technology or the Company may elect to enter into such a licence in order to settle litigation or in order to resolve disputes prior to litigation. However, the Company may not be able to obtain any required licence on commercially reasonable terms or at all. Even if the Company is able to obtain a licence, it could be non-exclusive, thereby giving its competitors access to the same technologies licensed to the Company, and could require the Company to make substantial royalty payments. The Company could also be forced, including by court order, to cease commercialising the infringing technology or products. A finding of infringement could prevent the Company from commercialising its products or force the Company to cease some of its business operations, which could materially harm its business. Claims that the Company has misappropriated the confidential information or trade secrets of third parties could have a similarly negative impact on its business.

Any such claims are likely to be expensive to defend, and some of its competitors may be able to sustain the costs of complex patent litigation more effectively than the Company can because they have substantially greater resources. Moreover, even if the Company is successful in defending any infringement proceedings, it may incur substantial costs and divert management's time and attention in doing so, which could materially adversely affect the Company's business, results of operations or financial condition.

3.5 If PTL fails to comply with its obligations under the MRC Licence, PTL could lose its rights to intellectual property, which is important to the business.

PTL is party to the MRC Licence under which it is granted rights to intellectual property relating to PT20. The MRC Licence imposes on PTL various development and commercialisation obligations as well as the requirement to pay royalties on sales of products and one-off payments on the attainment of certain milestones (amongst other obligations). The MRC has the right to terminate the MRC Licence if, *inter alia*, PTL commits a material breach of the licence and fails to remedy it within 30 days of notice of the breach. The termination of the MRC Licence would prevent PTL from using the licensed intellectual property and therefore prevent the Group from developing and commercialising PT20. In addition, if the MRC fails to prosecute or maintain some or all of the licensed patents, and fails to notify PTL such that PTL cannot itself prosecute or maintain such licensed patents, then the patent protection would lapse. Consequently, this would prevent PTL from enforcing such patents against third parties.

4 Risks relating to managing growth, employee matters and other risks relating to the Company's business

4.1 Growth may place significant demands on the Company's management and resources.

The Company expects to experience growth in the number of its employees and the scope of its operations in connection with the continued development and commercialisation of its products.

In particular, the Company plans to establish its own central and regional commercial functions including directly owned and managed sales and marketing capabilities to promote Feraccru and subsequently PT20 and other products if and when they are approved for commercial sale.

This potential growth will place a significant strain on its management and operations, and the Company may have difficulty managing this future potential growth.

4.2 The Company is dependent on its current management team.

The Company is highly dependent on its current management team. The services of the Company's management team are critical to the successful implementation of its product development and regulatory strategies. Whilst suitable contracts of employment are in place including six to twelve months' notice periods for all senior management, members of the Company's management team may give notice to terminate their employment with the Company at any time. The loss of the services of any of the Company's management team and its inability to find suitable replacements could harm its business, financial condition, prospects and ability to achieve the successful development or commercialisation of its products.

4.3 Challenges in identifying and retaining key personnel could impair the Company's ability to conduct and grow its operations effectively.

The Company's ability to compete in the highly competitive pharmaceutical industry depends upon its ability to attract and retain highly qualified management and sales teams. The Group is intending to recruit its own commercial team and expand its existing central infrastructure team. Many of the other pharmaceutical companies and academic institutions that it competes against for qualified personnel have greater financial and other resources, different risk profiles and a longer history in the industry than the Company does.

The Company might not be able to attract or retain these key persons on conditions that are economically acceptable. The inability of the Company to attract and retain these key persons could have a material adverse effect on its business, earnings, financial situation and prospects.

4.4 The Company may become subject to product liability claims.

The Company faces an inherent risk of product liability and associated adverse publicity as a result of the clinical testing of its products and sales of its products once marketing approval is received.

Criminal or civil proceedings might be filed against the Company by study subjects, patients, the regulatory authorities, pharmaceutical companies and any other third party using or marketing its products. Any such product liability claims may include allegations of defects in manufacturing, defects in design, negligence, strict liability, a breach of warranties and a failure to warn of dangers inherent in the product.

If the Company cannot successfully defend itself against product liability claims, it may incur substantial liabilities or be required to limit commercialisation of its products, if approved. Even successful defence could require significant financial and management resources.

Regardless of the merits or eventual outcome, liability claims may result in:

(a) decreased demand for its products due to negative public perception;

(b) injury to the Company's reputation;

(c) withdrawal of clinical study participants or difficulties in recruiting new study participants;

(d) initiation of investigations by regulators;

(e) costs to defend or settle the related litigation;

(f) diversion of management's time and the Company's resources;

(g) substantial monetary awards to patients, study participants or subjects;

(h) product recalls, withdrawals or labelling, marketing or promotional restrictions;

(i) loss of revenues from product sales; or

(j) the inability to commercialise any of the Group's products, if approved.

Although the Company maintains a level of insurance which is customary for its industry to cover its current business, any claim that may be brought against the Company could result in a court judgment or settlement in an amount that is not covered, in whole or in part, by its insurance or that is in excess of the limits of its insurance coverage. Its insurance policies also have various exclusions, and the Company may be subject to a product liability claim for which the Company has no coverage. In such cases, the Company would have to pay any amounts awarded by a court or negotiated in a settlement that exceed its coverage limitations or that are not covered by its insurance, and the Company may not have, or be able to obtain, sufficient capital to pay such amounts.

If the Company or its partners, licensees and subcontractors were unable to obtain and maintain appropriate insurance coverage at an acceptable cost, or to protect itself in any way against actions for damages, this would seriously affect the marketing of the Company's products and, more generally, be detrimental to its business, earnings, financial situation and growth prospects.

4.5 The Company's employees, contractors, consultants and commercial partners may engage in misconduct or other improper activities, including non-compliance with regulatory standards.

The Company is exposed to the risk of employees, independent contractors, principal investigators, consultants, commercial partners or vendors engaging in fraud or other misconduct. Misconduct could include intentional failures to comply with FDA or EMA regulations, to provide accurate information to the FDA or EMA or to comply with manufacturing standards the Company has established.

In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, bribery and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programmes and other business arrangements.

Employee misconduct could also involve the improper use of information obtained in the course of clinical studies, which could result in regulatory sanctions and serious harm to the Company's reputation. It is not always possible to identify and deter employee misconduct, and the precautions the Company takes to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting the Company from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. If any such actions are instituted against the Company, and the Company is not successful in defending itself or asserting its rights, those actions could have a significant impact on its business, including the imposition of significant fines or other sanctions, and its reputation.

4.6 The Company may be vulnerable to disruptions of information technology systems or breaches of data security

The Company is dependent on information technology systems and infrastructure to operate its business. In the ordinary course of its business, the Company collects, stores and transmits confidential information, including intellectual property, proprietary business information and personal information. It is important that the Company does so in a secure manner to maintain confidentiality and integrity of such confidential information. Any failure to do so could adversely affect the Company's business.

5 Risks Relating to the Placing, the Ordinary Shares and the Warrants

5.1 A liquid market for the Ordinary Shares and Warrants may fail to develop.

Prior to the Placing, there has been no public trading market for the Ordinary Shares or Warrants. The Placing Price has been agreed between Liberum and the Company and may not be indicative of the market price for the Ordinary Shares and Warrants following Admission.

Although the Company will apply to the London Stock Exchange for admission of the Ordinary Shares and Warrants to trading on AIM, an active trading market for the Ordinary Shares and Warrants may not develop or, if developed, may not be sustained following Admission. If an active trading market is not developed or maintained, the liquidity and trading price of the Ordinary Shares and Warrants could be materially and adversely affected.

5.2 The value of the Ordinary Shares and Warrants may fluctuate significantly and investors could lose all or part of their investment.

The share price of quoted companies can be highly volatile, for smaller pharmaceutical companies in particular, which may prevent Shareholders from being able to sell their Ordinary Shares at or above the price they paid for them. The Placing Price may not be indicative of prices that will prevail in the trading market and investors may not be able to resell the Ordinary Shares at or above the price they paid for them. The market price for the Ordinary Shares and Warrants could fluctuate significantly for various reasons, many of which are outside the Company's control. These factors could include the performance of the Company, large purchases or sales of the Ordinary Shares, legislative changes and general economic, political or regulatory conditions.

It is possible that the Company may decide to offer additional Ordinary Shares or convertible equity securities in the future to raise financing and for other purposes, including in connection with share incentive and share option plans. Future issues or the availability for issue of substantial amounts of the Ordinary Shares could dilute the holdings of Shareholders, adversely affect the prevailing market price of the Ordinary Shares and Warrants and impair the Company's ability to raise capital through future issues of Ordinary Shares.

5.3 The market price of the Ordinary Shares and Warrants could be negatively impacted by sales of substantial numbers of Ordinary Shares following the expiry of the lock-up period.

Pursuant to the Lock-up Agreements, the Locked-up Shareholders have agreed that, subject to certain exceptions, during the period of up to 12 months from the date of Admission, it/they will not issue, offer, sell or contract to sell, or otherwise dispose of any Ordinary Shares and Warrants (or any interest therein in respect thereof) or enter into any transaction with the same economic effect as any of the foregoing. Sales of a substantial number of Ordinary Shares by the Locked-up Shareholders after these restrictions expire, or the knowledge that they will, or the perception that these sales may occur, could depress the market price of the Ordinary Shares and the Warrants and could impair the Company's ability to raise capital through the sale of additional equity securities.

5.4 The Company does not currently anticipate paying dividends and, accordingly, Shareholders must rely on capital appreciation for any return on investment.

The Company currently intends to retain all of its future earnings, if any, to finance the growth and development of its business.

Under English law, a company can only pay cash dividends to the extent that it has distributable reserves and cash available for this purpose. The Company may not pay dividends if the Directors believe this would cause the Company to be inadequately capitalised or if, for any other reason, the Directors conclude it would not be in the best interests of the Company. The Company's direct and indirect subsidiaries may be precluded from paying dividends by various factors, such as their own financial condition, restrictions in existing or future financing documents to which they are party or applicable law. Any of the foregoing could limit the payment of dividends to Shareholders or, if the Company does pay dividends, the amount of such dividends. Any return to Shareholders will therefore be limited to the capital appreciation of their investment (if any) for the foreseeable future.

5.5 W.Health will retain a significant interest in the Company following Admission and its interests may differ from those of the other Shareholders

Following Admission, W.Health will hold over 49.99 per cent. of the Company's issued share capital and will, in addition, hold 1,945,640 Warrants. As a result, W. Health will possess sufficient voting power to maintain significant influence over all matters requiring the approval of Shareholders, including the election of directors and approval of significant corporate transactions. It will be able to block a special resolution of the Company. The interests of W. Health may not always be aligned with those of other holders of Ordinary Shares. Although W. Health has entered into the Relationship Agreement with the Company in order to govern certain aspects of its conduct in relation to the Company, that agreement may not be sufficient to safeguard the interests of other Shareholders.

W Health may make acquisitions of, or investments in, other businesses in the same sectors as the Company. These businesses may be, or may become competitors of the Company.

5.6 Shareholders outside the United Kingdom may not be able to participate in future equity offerings.

The Companies Act 2006 provides for pre-emptive rights to be granted to shareholders in the Company, unless such rights are disapplied by a special resolution of Shareholders. However, securities laws of certain jurisdictions may restrict the Company's ability to allow the participation of Shareholders in future offerings. In particular, Shareholders in the United States may not be entitled to exercise these rights unless either the rights and securities are registered under the Securities Act, or the rights and securities are offered pursuant to an exemption from, or in transactions not subject to, the registration requirements of the Securities Act. Any Shareholder who is unable to participate in future equity offerings may suffer dilution.

5.7 Shareholders may have difficulty in effecting service of process on the Company or the Directors in the United States, in enforcing U.S. judgments in the United Kingdom or in enforcing U.S. federal securities laws in UK courts.

The Company is incorporated outside the United States and substantially all of its assets are located outside the United States. As a result, it may not be possible for Shareholders to effect service of process within the United States upon all of the Directors or on the Company, or to obtain discovery of relevant documents and/or the testimony of witnesses. U.S. Shareholders may have difficulties enforcing in courts outside the U.S., judgments obtained in U.S. courts against some of the Directors or the Company (including actions under the civil liability provisions of the U.S. federal securities laws). Shareholders may also have difficulty enforcing liabilities under the U.S. federal securities laws in legal actions originally brought in jurisdictions located outside the United States.

5.8 Tax considerations

Changes in tax laws or subordinate legislation or the practice of any taxation authority could have a material adverse effect on the Company. An investment in the Company may involve complex tax considerations which may differ for each investor and each investor is advised to consult its own tax advisers. Any tax legislation and its interpretation and the legal and regulatory regimes which apply in relation to an investment in the Company may change at any time.

Investors should refer to the paragraph entitled ''UK taxation'' in paragraph 11 of Part 10 (*Additional Information*) for a summary of the possible tax consequences of owning the Ordinary Shares and Warrants.

5.9 Securities traded on AIM

The Ordinary Shares and Warrants will be traded on AIM rather than on the Official List. An investment in shares traded on AIM may carry a higher risk than an investment in shares listed on the Official List. Investors should be aware that the value of the Ordinary Shares and Warrants may be volatile and may go down as well as up and investors may therefore not recover their original investment especially since the market in the Ordinary Shares and Warrants on AIM may have limited liquidity.

The price at which investors may dispose of Ordinary Shares and Warrants may be influenced by a number of factors some of which may pertain to the Company and others of which are extraneous. Investors may realise less than the original amount invested.

5.10 Conditionality of the Placing

The Placing is conditional upon, among other things, Admission. In the event that any condition to which Admission is subject is not satisfied or, if capable of waiver, waived, Admission will not be implemented.

5.11 There is no guarantee that the Company will maintain its quotation on AIM

The Company cannot assure investors that the Company will always retain a quotation on AIM. Additionally, if in the future the Company decides to obtain a listing or quotation on another exchange in addition to AIM, the level of liquidity of the Ordinary Shares and Warrants traded on AIM could decline.

5.12 Suitability

Investment in the Ordinary Shares and Warrants may not be suitable for all readers of this document. Readers are accordingly advised to consult your stockbroker, bank manager, solicitor or accountant or other independent financial adviser, being (in the case of persons resident in the United Kingdom) an organisation or firm authorised pursuant to FSMA who specialises in investments of this nature before making any investment decision.

PART 4

UNAUDITED PRO FORMA FINANCIAL INFORMATION

Section A: Introduction

The unaudited *pro forma* financial information set out below has been prepared to illustrate the effect of the acquisition of the PTL and SHG and the Placing proceeds receivable by the Company on the consolidated net assets of the Company as if they had taken place on 30 June 2015 and on the consolidated income statement of the Company as if they had taken place on 1 January 2014. The unaudited *pro forma* financial information has been prepared on the basis of, and should be read in conjunction with, the notes set out below.

The unaudited *pro forma* statement of net assets of the Company is based on the consolidated net assets of the SHG Group and Phosphate Therapeutics as at 30 June 2015 and has been prepared on the basis that the acquisition of the SHG Group and Phosphate Therapeutics and the proceeds raised through the Placing were effective as of 30 June 2015. The unaudited *pro forma* statement of net assets has been prepared in a manner consistent with the accounting policies to be adopted by the Company for the year ending 31 December 2015.

The unaudited *pro forma* income statement of the Company is based on the consolidated profits of the SHG Group and Phosphate Therapeutics for the year ended 31 December 2014 and has been prepared on the basis that the acquisition of the SHG Group and Phosphate Therapeutics and the proceeds of the Placing were effective as of 1 January 2014. The unaudited *pro forma* income statement has been prepared in a manner consistent with the accounting policies to be adopted by the Company for the year ending 31 December 2015.

Because of its nature, the unaudited *pro forma* financial information addresses a hypothetical situation and, therefore, does not represent the Company's actual financial position or results. It may not, therefore, give a true picture of the Company's financial position or results nor is it indicative of the results that may, or may not, be expected to be achieved in the future. The *pro forma* financial information has been prepared for illustrative purposes only in accordance with Annex II of the Prospectus Directive.

Section B: Unaudited *pro forma* statement of net assets of Shield Therapeutics plc

£'000	Shield Therapeutics plc *Note 1*	SHG *Note 2*	PTL *Note 3*	Adjustments *Note 4*	*Note 5*	*Note 6*	*Note 7*	*Note 8*	Unaudited Proforma
Non-current assets									
Intangible assets		494	833						1,327
Property plan and equipment		20							20
	—	514	833						1,347
Current assets									
Other receivables		140	61	(44)					157
Cash and cash equivalents		3,663	767					32,500	36,930
	—	3,803	828	(44)					37,087
Total assets	**—**	**4,317**	**1,661**	**(44)**					**38,434**
Current liabilities									
Trade and other payables		(1,023)	(849)	44				(2,421)	(4,249)
Interest bearing loans and borrowings		(12,107)	(12,477)		12,107		12,477		—
Other liabilities		(41)							(41)
	—	(13,171)	(13,326)	44	12,107		12,477		(4,290)
Non current liabilities									
Other financial liabilities		(39,619)				39,619			—
Total liabilities	**—**	**(52,790)**	**(13,326)**	**44**	**12,107**	**39,619**	**12,477**		**(4,290)**
Net assets/(liabilities)	**—**	**(48,473)**	**(11,665)**		**12,107**	**39,619**	**12,477**		**34,144**

Notes

1. Shield Therapeutics plc was incorporated on 3 September 2015 and has not traded from incorporation to the date of this document. No historical financial information has been prepared for Shield Therapeutics plc.
2. The net assets of SHG Group have been extracted without adjustment from the historical financial information set out in Part 5 *(Historical Financial Information for Shield Holdings)*.
3. The net assets of PTL have been extracted without adjustment from the historical financial information set out in Part 6 *(Historical Financial Information for Phosphate Therapeutics)*.
4. The adjustment in Note 4 reflects the elimination of inter-company balances held between SHG Group and PTL in respect of management fees charged by the SHG Group to PTL which will be eliminated on consolidation by Shield Therapeutics plc.
5. The adjustment in Note 5 reflects the recategorisation of shareholder debt as equity in SHG Group. This will be eliminated as a result of the Corporate Reorganisation prior to Admission.
6. The adjustment in Note 6 reflects the elimination of derivative liabilities held in SHG Group in respect of shareholder debt at fair value which will be eliminated as a result of the Corporate Reorganisation prior to Admission.
7. The adjustment in Note 7 reflects the recategorisation of shareholder debt as equity in PTL. This will be eliminated as a result of the Corporate Reorganisation prior to Admission.
8. The adjustment in Note 8 reflects the net proceeds of the Placing receivable by the Company comprising gross proceeds of £32.5 million including estimated transaction costs of £2.4 million and the settlement of the transaction fees accrued at 30 June 2015.

Section C: Unaudited *pro forma* income statement of Shield Therapeutics plc

£'000	Shield Therapeutics plc *Note 1*	SHG *Note 2*	PTL *Note 3*	Adjustments *Note 4*	Adjustments *Note 5*	Adjustments *Note 6*	Adjustments *Note 7*	Adjustments *Note 8*	Unaudited Proforma 2014 Total
Other operating income	—	244		(244)					
Clinical study costs		(1,069)	(2,224)						(3,293)
Manufacturing		(249)	(287)						(536)
Regulatory		(340)	(38)						(378)
Indirect Personnel		(831)	(261)	244					(848)
Share based payments		(179)	0		179				
Total other operating Expenses	—	(2,668)	(2,810)	244	179				(5,055)
Administrative expenses		(967)	(207)						(1,174)
Operating loss	—	(3,391)	(3,017)		179				(6,229)
Financial Income		206				(206)			0
Net loss on financial instruments designated as fair value through profit or loss		(8,585)						8,585	0
Financial expenses		(1,660)	(1,700)			1,367	1,631		(362)
Loss before tax	—	(13,430)	(4,717)	0	179	1,161	1,631	8,585	(6,591)
Taxation		0	(280)						(280)
Loss for the period	—	(13,430)	(4,997)	0	179	1,161	1,631	8,585	(6,871)

Notes

1. Shield Therapeutics plc was incorporated on 3 September 2015 and has not traded from incorporation to the date of this document. No historical financial information has been prepared for Shield Therapeutics plc.
2. The net income of SHG Group has been extracted without adjustment from the historical financial information set out in Part 5 *(Historical Financial Information for Shield Holdings).*
3. The net income of PTL has been extracted without adjustment from the historical financial information set out in Part 6 *(Historical Financial Information for Phosphate Therapeutics).*
4. The other operating income for SHG Group and other operating expenses for PTL include an arm's length services agreement between SHG's subsidiary ITU and PTL. This has been extracted without adjustment from the historical financial information set out in Part 5 and Part 6 as this operating agreement was agreed to be terminated conditional on Admission.
5. The other operating expenses for SHG included share based payments. The costs have been extracted without adjustment from the historical financial information for SHG as set out in Part 5 (*Historical Financial Information for Shield Holdings*) as they represent one off costs from historic option schemes that crystallised as a result of Admission. Going forward there is expected to be a charge to the income statement as a result of the issue of options under the Company's new option schemes.
6. The adjustment in Note 6 relates to the classification of certain shareholder investments in SHG as debt as these investments have been converted to ordinary equity in the Company prior to Admission. The costs which are taken from the underlying books and records of SHG have therefore been eliminated.
7. The adjustment in Note 7 relates to the classification of certain shareholder investments in PTL as debt as these investments have been converted to ordinary equity in the Company on Admission. These costs, which have been extracted from the underlying books and records of PTL have therefore been eliminated and this elimination will not be required after Admission.
8. The adjustment in Note 8 reflects the elimination of derivative instruments held in SHG Group in respect of shareholder debt at fair value which will be eliminated as a result of the Corporate Reorganisation prior to Admission.
9. The adjustments in Note 4, 6, 7 and 8 will have no continuing impact on the statements of the Company going forward.

PART 5

HISTORICAL FINANCIAL INFORMATION FOR SHIELD HOLDINGS AG

Section A: Accountant's report on consolidated historical information on SHG

The Directors
Shield Therapeutics plc
Northern Design Centre
Studio 6, 3rd Floor
Baltic Business Quarter
Gateshead Quays
NE8 3DF

12 February 2016

Ladies and Gentlemen

Shield Therapeutics plc – Shield Holdings AG

We report on the consolidated financial information set out on pages 89 to 118 for the three years and six months ended 30 June 2015. This financial information has been prepared for inclusion in the Admission Document dated 12 February 2016 of Shield Therapeutics plc on the basis of the accounting policies set out in note 2. This report is required by Paragraph (a) of Schedule Two of the AIM Rules for Companies and is given for the purpose of complying with that paragraph and for no other purpose. We have not audited or reviewed the financial information for the six months ended 30 June 2014 which has been included for comparative purposes only, and accordingly do not express an opinion thereon.

Responsibilities

The Directors of Shield Therapeutics plc are responsible for preparing the financial information on the basis of preparation set out in note 2 to the financial information and in accordance with International Financial Reporting Standards as adopted by the European Union.

It is our responsibility to form an opinion on the financial information and to report our opinion to you.

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

Basis of opinion

We conducted our work in accordance with Standards for Investment Reporting issued by the Auditing Practices Board in the United Kingdom. Our work included an assessment of evidence relevant to the amounts and disclosures in the financial information. It also included an assessment of the significant estimates and judgments made by those responsible for the preparation of the financial information and whether the accounting policies are appropriate to the entity's circumstances, consistently applied and adequately disclosed.

We planned and performed our work so as to obtain all the information and explanations 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 on financial information

In our opinion, the consolidated financial information gives, for the purposes of the Admission Document dated 12 February 2016, a true and fair view of the state of affairs of Shield Holdings AG as at 31 December 2012, 2013 and 2014 and 30 June 2015 and of its consolidated losses, consolidated comprehensive income, consolidated cash flows and consolidated changes in equity for the three years and six months ended 30 June 2015 in accordance with the basis of preparation set out in note 2 and in accordance with International Financial Reporting Standards as adopted by the European Union.

Declaration

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

Yours faithfully

KPMG LLP

Section B: Consolidated historical financial information

Consolidated Statement of Profit and loss and Other Comprehensive Income

	Note	Year ended 31 December 2012	Year ended 31 December 2013	Year ended 31 December 2014	6 months to 30 June 2014 (unaudited)	6 months to 30 June 2015
		£000	£000	£000	£000	£000
Other operating income		203	244	244	124	120
Research and development expenditure	*7*	(3,370)	(3,123)	(2,668)	(1,192)	(1,215)
Administrative expenses	*7*	(438)	(963)	(967)	(384)	(574)
Operating loss		(3,605)	(3,842)	(3,391)	(1,452)	(1,669)
Financial income	*10*	650	591	206	360	1,890
Net loss on financial instruments designated as fair value through profit or loss		—	—	(8,585)	(9,842)	(28,949)
Financial expense	*10*	(505)	(1,266)	(1,660)	(832)	(1,299)
Loss before tax		(3,460)	(4,517)	(13,430)	(11,766)	(30,027)
Taxation	*12*	—	—	—	—	—
Loss for the period		(3,460)	(4,517)	(13,430)	(11,766)	(30,027)
Attributable to:						
Equity holders of the parent		(3,147)	(4,189)	(12,905)	(11,534)	(29,611)
Non-controlling interests		(313)	(328)	(525)	(232)	(416)
Other comprehensive income						
Items that are or may be reclassified subsequently to profit or loss:						
Foreign currency translation differences – foreign operations		(71)	41	248	(100)	(295)
Total comprehensive income for the period		(3,531)	(4,476)	(13,182)	(11,866)	(30,322)
Attributable to:						
Equity holders of the parent		(3,218)	(4,148)	(12,657)	(11,634)	(29,906)
Non-controlling interests		(313)	(328)	(525)	(232)	(416)
Basic and diluted loss per share	*11*	(6.8p)	(8.9p)	(26.5p)	(23.2p)	(59.3p)

Consolidated balance sheet

	Note	31 December 2012	31 December 2013	31 December 2014	30 June 2014 (unaudited)	30 June 2015
		£000	£000	£000	£000	£000
Non-current assets						
Intangible assets	*14*	321	387	436	426	494
Property, plant and equipment	*13*	5	5	12	4	20
		326	392	448	430	514
Current assets						
Other receivables	*15*	124	101	79	255	140
Cash and cash equivalents	*16*	4,004	1,550	477	1,573	3,663
		4,128	1,651	556	1,828	3,803
Total assets		4,454	2,043	1,004	2,258	4,317
Current liabilities						
Trade and other payables	*17*	(903)	(919)	(694)	(544)	(1,023)
Interest bearing loans and borrowings	*18*	(4,843)	(7,093)	(8,258)	(7,632)	(12,107)
Other liabilities		(80)	(36)	(50)	(50)	(41)
		(5,826)	(8,048)	(9,002)	(8,226)	(13,171)
Non-current liabilities						
Interest bearing loans and borrowings	*18*	—	—	(197)	—	(891)
Other financial liabilities	*19*	(1,871)	(1,312)	(10,089)	(11,129)	(38,728)
		(1,871)	(1,312)	(10,286)	(11,129)	(39,619)
Total liabilities		(7,697)	(9,360)	(19,288)	(19,355)	(52,790)
Net liabilities		(3,243)	(7,317)	(18,284)	(17,097)	(48,473)
Equity						
Share capital	*23*	365	365	365	365	365
Share premium		2,393	2,393	2,393	2,393	2,393
Currency translation reserve		(71)	(30)	218	(130)	(77)
Retained earnings		(7,005)	(10,792)	(23,006)	(21,764)	(52,484)
Equity attributable to owners of the parent		(4,318)	(8,064)	(20,030)	(19,136)	(49,803)
Non-controlling interest		1,075	747	1,746	2,039	1,330
Total equity		(3,243)	(7,317)	(18,284)	(17,097)	(48,473)

Consolidated statement of changes in equity

	Issued capital	Share premium	Currency translation reserve	Retained earnings	Non-controlling Interest	Total
	£000	£000	£000	£000	£000	£000
At 1 January 2012	365	2,393	—	(4,358)	1,388	(212)
Loss for the year	—	—	—	(3,147)	(313)	(3,460)
Other comprehensive income	—	—	(71)	—	—	(71)
Equity-settled share based payment transactions	—	—	—	500	—	500
Balance at 31 December 2012	365	2,393	(71)	(7,005)	1,075	(3,243)
Loss for the year	—	—	—	(4,189)	(328)	(4,517)
Other comprehensive income	—	—	41	—	—	41
Equity-settled share based payment transactions	—	—	—	402	—	402
Balance at 31 December 2013	365	2,393	(30)	(10,792)	747	(7,317)
Loss) for the year	—	—	—	(12,905)	(525)	(13,430)
Other comprehensive income	—	—	248	—	—	248
Additional investment of non-controlling interest shareholder	—	—	—	—	1,968	1,968
Increase in non-controlling interest*	—	—	—	444	(444)	—
Equity-settled share based payment transactions	—	—	—	247	—	247
Balance at 31 December 2014	365	2,393	218	(23,006)	1,746	(18,284)
Balances at 1 January 2014	365	2,393	(30)	(10,792)	747	(7,317)
Loss for the period	—	—	—	(11,534)	(232)	(11,766)
Other comprehensive income/ (expense)	—	—	(100)	—	—	(100)
Additional investment of non-controlling interest shareholder	—	—	—	—	1,968	1,968
Increase in non-controlling interest*	—	—	—	444	(444)	—
Equity-settled share based payment transactions	—	—	—	118	—	118
Balance at 30 June 2014	365	2,393	(130)	(21,764)	2,039	(17,097)
Balances at 1 January 2015	365	2,393	218	(23,006)	1,746	(18,284)
Loss for the period	—	—	—	(29,611)	(416)	(30,027)
Other comprehensive income/ (expense)	—	—	(295)	—	—	(295)
Equity-settled share based payment transactions	—	—	—	133	—	133
Balance at 30 June 2015	365	2,393	(77)	(52,484)	1,330	(48,473)

* Increase in non-controlling interest relates to the additional investment of £1,968,000 of non-controlling interest shareholder, resulting in the non-controlling interest ownership increasing from 8.60% to 16.47% in 2014.

Consolidated statement of cash flows

	Year ended 31 December 2012	Year ended 31 December 2013	Year ended 31 December 2014	6 months to 30 June 2014 (unaudited)	6 months to 30 June 2015
	£000	£000	£000	£000	£000
Cash flows from operating activities					
Loss for the period	(3,460)	(4,517)	(13,430)	(11,766)	(30,027)
Adjustments for :					
Depreciation and amortisation	28	32	36	1	27
(Gain)/loss) on derivative financial instruments	(532)	(569)	8,585	9,842	28,949
Equity-settled share based payment expenses	500	402	247	118	133
Financial expense	505	1,266	1,660	832	1,299
Unrealised foreign exchange (gains)/loss	(184)	121	(250)	(417)	(1,923)
	(3,143)	(3,265)	(3,152)	(1,390)	(1,542)
Decrease/(increase) in trade and other receivables	140	23	22	(154)	(61)
Increase/(decrease):					
Trade and other payables	39	16	(225)	(375)	329
Other liabilities	68	(44)	14	14	(9)
Net cash flow from operating activities	(2,896)	(3,270)	(3,341)	(1,905)	(1,283)
Cash flows from investing activities					
Acquisitions of intangible assets	(52)	(98)	(80)	(40)	(84)
Acquisition of property, plant and equipment	—	—	(12)	—	(10)
Net cash from investing activities	(52)	(98)	(92)	(40)	(94)
Cash flows from financing activities					
Investment of non-controlling interest shareholder	—	—	1,968	1,968	—
Issuance of convertible bonds	—	—	392	—	1,062
Issuance of preference shares	3,436	914	—	—	3,501
Net cash flow from financing activities	3,436	914	2,360	1,968	4,563
Net increase/(decrease) in cash	488	(2,454)	(1,073)	23	3,186
Cash and cash equivalents at 1 January	3,516	4,004	1,550	1,550	477
Cash and cash equivalents at period end	4,004	1,550	477	1,573	3,663

Notes
(forming part of the financial statements)

1 General information

Shield Holdings, AG (''SHG'') was incorporated in Switzerland on 19 October 2010.

SHG is domiciled in Switzerland and the registered office of SHG is Sihleggstrasse 23, Wollerau 8832, Switzerland.

SHG is the parent entity that holds investments in a number of subsidiaries. Its trading subsidiaries are engaged in the development of clinical state pharmaceutics to treat unmet medical needs.

Subsidiaries and their countries of incorporation are presented in note 24.

2 Accounting policies

As detailed in paragraph 2 of Part 10 (*Additional Information*) of this Admission Document, in preparation for Admission the Group undertook a corporate reorganisation that will result in the Company, Shield Therapeutics plc, becoming the ultimate holding company of the Group. The corporate reorganisation steps comprise, amongst other things, the Company acquiring the entire issued share capital of SHG and, conditional upon Admission, the entire issued share capital of PTL. Whilst the Company is the legal acquirer, for accounting purposes the financial statements of the Company will be a continuation of SHG.

The financial information is presented on the basis of the accounting policies and practices of SHG as will be applied in the first published financial statements following Admission. It has not been prepared on the basis that the Corporate Reorganisation has completed. This Part 5 (*Historical financial information for Shield Holdings*) of the Admission Document includes information on the SHG Group and Part 6 (*Historical financial information for Phosphate Therapeutics*) of this Admission Document includes information on Phosphate Therapeutics Limited.

The financial information has been prepared for the purposes of the Admission Document in accordance with the requirements of Paragraph (a) of Schedule Two of the AIM Rules for Companies and in accordance with IFRS as adopted by the EU (EU-IFRS) and this basis of preparation, including the significant accounting policies, is set out below.

The directors of SHG are responsible for the preparation of this financial information.

The consolidated company financial statements have been prepared and approved by the directors in accordance with International Financial Reporting Standards as adopted by the EU (''Adopted IFRSs'').

The accounting policies set out below have, unless otherwise stated, been applied consistently to all periods presented in these financial statements.

The financial statements are prepared on the historical cost basis except for derivative financial instruments that are stated at their fair value.

The functional currency of the SHG is GBP. The consolidated financial statements are presented in GBP and all values are rounded to the nearest thousand (£000), except otherwise indicated.

Going concern

The SHG Group funds the development of its products and meets its day to day working capital requirements from cash reserves and shareholder funding in the form of equity and preference shares and shareholder loans. As more fully described in notes 18 and 22, whilst elements of shareholder funding have historically been treated as debt, the terms have been designed to ensure that any cash payments of interest or capital would only fall due when the SHG Group has sufficient funds. As explained in note 29 the SHG Group has entered into an agreement with the shareholders that, conditional upon Admission, all of the shareholder debt, including any accrued interest, will be replaced with Ordinary Shares. As a result the Group would be debt free at the time of Admission.

As at 30 June 2015 the SHG Group had cash resources of £3,663,000.

The Directors have prepared cash flow forecasts for a period that exceeds 12 months from the date of authorisation of these financial statements. These forecasts include estimates of both the costs and timing of the successful commercialisation of the SHG Group's products. The Directors, taking into account the potential impact of delays and/ or cost overruns in those forecasts, are

confident that the Placing would raise sufficient funds to bring the SHG Group's products to a stage where they can generate significant revenues.

In the preparation of this Historical Financial Information, the Directors have assumed that the Placing will be completed as described elsewhere in this Admission Document. On the assumption of a successful completion of the Placing, the Directors are confident that the SHG Group will have sufficient resources to meet cash requirements for at least the 12 months following the date of approval of this report and accordingly have adopted the going concern basis in the preparation of this Historical Financial Information.

Basis of consolidation

The consolidated financial statements comprise the financial statements of the SHG Group and its subsidiaries as at 31 December 2014.

Subsidiaries are fully consolidated from the date of acquisition, being the date on which the SHG Group obtains control, and continue to be consolidated until the date when such control ceases. The financial statements of the subsidiaries are prepared for the same reporting period as the parent company, using consistent accounting policies. All intra-group balances, transactions, unrealised gains and losses resulting from intra-group transactions and dividends are eliminated in full.

Losses within a subsidiary are attributed to the non-controlling interest even if that results in a deficit balance. A change in the ownership interest of a subsidiary, without a loss of control, is accounted for as an equity transaction.

Foreign currency

Transactions in foreign currencies are translated to SHG's functional currency at the foreign exchange rate ruling at the date of the transaction. Monetary assets and liabilities denominated in foreign currencies at the balance sheet date are retranslated to the functional currency at the foreign exchange rate ruling at the date. Foreign exchange differences arising on translation are recognised in the income statement. Non-monetary assets and liabilities that are measured in terms of historical cost in a foreign currency are translated using the exchange rate at the date of the transaction. Non-monetary assets and liabilities denominated in foreign currencies that are stated at fair value are retranslated to the functional currency at foreign exchange rates ruling at the dates the fair value was determined.

Exchange differences relating to the translation from the functional currencies of the SHG Group's foreign subsidiaries into GBP are accounted for by entries made directly to the foreign currency translation reserve.

Classification of financial instruments issued by SHG

Following the adoption of IAS 32, financial instruments issued by SHG are treated as equity only to the extent that they meet the following two conditions:

- they include no contractual obligations upon the company to deliver cash or other financial assets or to exchange financial assets or financial liabilities with another party under conditions that are potentially unfavourable to the company; and
- where the instrument will or may be settled in the company's own equity instruments, it is either a non-derivative that includes no obligation to deliver a variable number of the company's own equity instruments or is a derivative that will be settled by the company's exchanging a fixed amount of cash or other financial assets for a fixed number of its own equity instruments.

To the extent that this definition is not met, the proceeds of issue are classified as a financial liability. Where the instrument so classified takes the legal form of the company's own shares, the amounts presented in these financial statements for called up share capital and share premium account exclude amounts in relation to those shares.

Where a financial instrument that contains both equity and financial liability components exists these components are separated and accounted for individually under the above policy.

Non-derivative financial instruments

Non-derivative financial instruments comprise other receivables, cash at bank and in hand, restricted cash, loans and borrowings, and trade and other payables.

Trade and other receivables

Trade and other receivables are recognised initially at fair value. Subsequent to initial recognition they are measured at amortised cost using the effective interest method, less any impairment losses.

Trade and other payables

Trade and other payables are recognised initially at fair value. Subsequent to initial recognition they are measured at amortised cost using the effective interest method.

Cash and cash equivalents

Cash and cash equivalents comprises cash balances in the bank and restricted cash.

Restricted Cash

This represents cash funding received from investors for the issuance of additional share capital. Under Swiss law shares can only be issued once the capital increase has been registered with the Swiss authorities. Where cash is received close to year end there is not sufficient time for the registration to go through prior to year end. As a result, the cash is held in a restricted account in line with Swiss law until the shares are issued.

Interest-bearing loans and borrowings

Interest-bearing loans and borrowings are recognised initially at fair value less attributable transaction costs. Subsequent to initial recognition, interest-bearing borrowings are stated at amortised cost using the effective interest method, less any impairment losses.

Embedded derivatives

Derivatives embedded in host contracts are accounted for as separate derivatives and recorded at fair value if their economic characteristics and risks are not closely related to those of the host contracts and the host contracts are not held for trading or designated at fair value through the profit or loss. These embedded derivatives are measured at fair value with changes in fair value recognised in profit or loss.

Intangible assets

Research and development

The SHG Group's activities are still considered to be in the research phase and therefore all related expenditure has been recognised as an expense in the income statement. As there has been no expenditure on development activities, there has been no capitalisation of research and development costs.

Expenditure in relation to patents registration and renewal of current patents are capitalised and recorded as intangible assets. Registration costs are continually incurred as the Group registers these patents in different countries. Intangible assets are stated at cost less accumulated amortisation and less accumulated impairment losses.

Amortisation

Amortisation is charged to the income statement on a straight-line basis over the estimated useful lives of the patents. Patent assets are amortised from the date they are available for use. The estimated useful life of the patent suite is until 2026.

Operating income

Other operating income is measured at the fair value of consideration received or receivable for management services supplied to related parties. Income is recognised when the service has been delivered.

Expenses

Financing income and expenses

Financing expenses comprise interest payable, finance charges on shares classified as liabilities and net foreign exchange losses that are recognised in the income statement (see foreign currency accounting policy). Financing income comprise interest receivable on funds invested, dividend income, and net foreign exchange gains.

Interest income and interest payable is recognised in profit or loss as it accrues, using the effective interest method. Dividend income is recognised in the income statement on the date the entity's right to receive payments is established. Foreign currency gains and losses are reported on a net basis.

Taxation

Tax on the profit or loss for the year comprises current and deferred tax. Tax is recognised in the income statement except to the extent that it relates to items recognised directly in equity, in which case it is recognised in equity.

Current tax is the expected tax payable or receivable on the taxable income or loss for the year, using tax rates enacted or substantively enacted at the balance sheet date, and any adjustment to tax payable in respect of previous years.

A deferred tax asset is recognised only to the extent that it is probable that future taxable profits will be available against which the temporary difference can be utilised.

Share-based payments

Employees of the SHG Group receive remuneration in the form of share-based payments, whereby employees render services as consideration for share options (equity-settled transactions).

The fair value of options granted is recognised as an employee expense with a corresponding increase in the share premium account. The fair value is measured at the grant date and spread over the period during which the employees become unconditionally entitled to the options. The fair value of the options granted is measured using an appropriate option pricing model, taking into account the terms and conditions upon which the options were granted. The amount recognised as an expense is adjusted to reflect the actual number of awards for which the related service and non-market vesting conditions are expected to be met, such that the amount ultimately recognised as an expense is based on the number of awards that do meet the related service and non-market performance conditions at the vesting date. For share-based payment awards with non-vesting conditions, the grant date fair value of the share-based payment is measured to reflect such conditions and there is no true-up for differences between expected and actual outcomes.

Share options have also been offered to contractors and suppliers of the SHG Group. The fair values of the option provided have been determined with reference to the fair value of the services provided to the Group.

3 Critical accounting judgements and key sources of estimation uncertainty

In the application of the SHG Group's accounting policies, which are described in note 2, management is required to make judgements, estimates and assumptions about the carrying amounts of assets and liabilities that are not readily apparent from other sources.

The estimates and underlying assumptions are reviewed on an ongoing basis. Revisions to accounting estimates are recognised in the period in which the estimate is revised if the revision affects only that period or in the period of the revision and future periods if the revision affects both current and future periods.

Share-based payment transactions

The SHG Group measures the cost of equity-settled transactions with employees by reference to the fair value of the equity instruments at the date at which they are granted. Estimating fair value for share-based payment transactions requires determining the most appropriate valuation model, which is dependent on the terms and conditions of the grant. This estimate also requires the determination of the most appropriate inputs to the valuation model including the expected life of the share option and volatility and making assumptions about them. The assumptions and models used for estimating fair value for share-based payment transactions are disclosed in note 25.

Fair value of derivative instruments

Where the fair value of derivative instruments recorded in the statement of financial position cannot be derived from active markets, their fair value is determined using valuation techniques. The inputs to these models are taken from observable markets where possible. Where this is not feasible, a degree of judgment is required in establishing fair values. The judgments include considerations of inputs such as entity value and volatility.

Deferred tax assets

Estimates of future profitability are required for the decision whether or not to create a deferred tax asset. To date no deferred tax assets have been recognised.

4 First-time adoption of IFRSs

These financial statements, for the year ended 31 December 2014, are the first the SHG Group has prepared in accordance with IFRSs. For periods up to and including the year ended 31 December 2014, the SHG Group prepared its financial statements in accordance with Swiss Code of Obligation (Schweizerisches Obligationenrecht). Accordingly, the SHG Group has prepared financial statements which comply with IFRSs applicable for periods ending on or after 31 December 2014, together with the comparative period data as at and for the year ended 31 December 2013 and 31 December 2012, as described in the accounting policies. In preparing these financial statements, the SHG Group's opening statement of financial position was prepared as at 1 January 2012, the SHG Group's date of transition to IFRSs. This note explains the principal adjustments made by the SHG Group in restating its Swiss GAAP statement of financial position as at 1 January 2012 and its previously published Swiss GAAP statement of financial performance for the year ended 31 December 2012.

Exemptions applied

IFRS 1: *First-Time Adoption of International Financial Reporting Standards*, allows first-time adopters certain exemptions from the retrospective application of certain IFRS. The SHG Group has applied the following exemptions:

- Cumulative currency translation differences for all foreign operations are deemed to be zero as at 1 January 2012.
- Share based payments – IFRS 2 is being applied to equity instruments that were granted after 7 November 2002 and that had not vested by 1 January 2012.

SHG Group reconciliation of equity as at 1 January 2012 (date of transition to IFRS)

	Notes	Swiss GAAP	Remeasure-ments	IFRS at 1 January 2012
		£000	£000	£000
Non-current assets				
Intangible assets		297	—	297
Property, plant and equipment		5	—	5
		302	—	302
Current assets				
Other receivables		262	—	262
Cash and cash equivalents		3,516	—	3,516
		3,778	—	3,778
Total assets		4,080	—	4,080
Current liabilities				
Trade and other payables		(865)	—	(865)
Interest-bearing loans and borrowings	B	—	(1,521)	(1,521)
Other liabilities	A	(93)	81	(12)
		(958)	(1,440)	(2,398)
Non-current liabilities				
Other financial liabilities	B	—	(1,894)	(1,894)
Total liabilities		(958)	(3,334)	(4,292)
Net assets/(liabilities)		3,122	(3,334)	(212)
Equity				
Share capital		365	—	365
Share premium	B	5,483	(3,090)	2,393
Retained earnings	A,B,C	(4,114)	(244)	(4,358)
Equity attributable to owners of the parent		1,734	(3,334)	(1,600)
Non-controlling interest		1,388	—	1,388
Total equity		3,122	(3,334)	(212)

SHG Group reconciliation of equity as at 31 December 2014

	Notes	Swiss GAAP	Remeasure-ments	IFRS at 31 December 2014
		£000	£000	£000
Non-current assets				
Intangible assets		436	—	436
Property, plant and equipment		12	—	12
		448	—	448
Current assets				
Other receivables		79	—	79
Cash and cash equivalents		477	—	477
		556	—	556
Total assets		1,004	—	1,004
Current liabilities				
Trade and other payables		(694)	—	(694)
Other financial liabilities	B	—	(8,258)	(8,258)
Other liabilities	A	(100)	50	(50)
		(794)	(8,208)	(9,002)
Non-current liabilities				
Interest-bearing loans and borrowings	D	(391)	194	(197)
Other financial liabilities	B	—	(10,089)	(10,089)
Total liabilities		(1,185)	(18,103)	(19,288)
Net assets/(liabilities)		(181)	(18,103)	(18,284)
Equity				
Share capital		365	—	365
Share premium	B	2,072	321	2,393
Currency translation reserve		7,979	(7,761)	218
Retained earnings	A,B,C,D	(12,343)	(10,663)	(23,006)
Equity attributable to owners of the parent		(1,927)	(18,103)	(20,030)
Non-controlling interest		1,746	—	1,746
Total equity		(181)	(18,103)	(18,284)

SHG Group reconciliation of statement of comprehensive income for the year ended 31 December 2014

	Notes	Swiss GAAP	Remeasure-ments	IFRS at 31 December 2014
		£000	£000	£000
Other operating income		244	—	244
Research and development expenditure		(2,680)	(179)	(2,859)
General and administration expenses	C	(738)	(38)	(776)
Operating loss		(3,174)	(217)	(3,391)
Financial income	D	—	206	206
Financial expense	B	(280)	(9,965)	(10,245)
Loss for the period		(3,454)	(9,976)	(13,430)
Other comprehensive income/(expense):				
Movements in currency translation reserve		248	—	248
Total comprehensive income/(expense) for the period		(3,206)	(9,976)	(13,182)

Notes to the reconciliation of equity as at 1 January 2012 and 31 December 2012 and total comprehensive income for the year ended 31 December 2014

A Risk shares

The Risk Shares liability relates to the share-based payments of the SHG Group awarded to its suppliers, recorded as liabilities based on the fair value of the services under Swiss GAAP. IFRS requires similar measurement requirements for the share-based payments expense but requires the transaction to be recorded as part of equity instead of liabilities.

B Preference shares

Preference shares are recorded as part of equity under Swiss GAAP, with no requirement to accrue for the interest component as the instrument is classified as equity. Under IFRS, these preference shares with redemption features are classified as financial liabilities with interest expense recognised using the effective interest method. Further, these preference shares carry a convertible feature which is required to be accounted for as a separate component from the host financial instrument and measured at fair value through profit or loss with adjustments taken up in financial expenses in profit or loss. These preference shares are denominated in Euro (see note 18).

C Share options

Share options are not recognised under Swiss GAAP until the option has been exercised. IFRS requires the expense and corresponding equity value of equity based share options offered to employees to be measured at the share option's fair value. For share options awarded to non-employees, the expense and corresponding equity value should be measured with reference to the fair value of the services received.

D Convertible bonds

Convertible bonds are measured under Swiss GAAP at their face value with simple interest accruing and without consideration of the attached convertible feature. IFRS requires that convertible features be accounted as a separate component of the host financial instrument and measured at fair value through profit or loss with adjustments taken up in financial expenses in profit or loss.

5 New standards and interpretations

The following new standard was effective from the period beginning 1 January 2014:

IFRS 13 Fair Value Measurement

IFRS 13 establishes a single source of guidance under IFRS for all fair value measurements. IFRS 13 does not change when an entity is required to use fair value, but rather provides guidance on how to measure fair value under IFRS. IFRS 13 defines fair value as an exit price. As a result of the guidance in IFRS 13, the Group has included the fair value measurement policy in Note 2 above.

The following standards and interpretations have an effective date after the date of these financial statements. The SHG Group has not early adopted them and plans to adopt them from the effective dates. Their adoption is not anticipated to have material effect on the financial statements.

Standard or interpretation	Title	Effective for accounting periods beginning on or after
AIP IFRS 2	Definition of vesting conditions	1 July 2014
AIP IAS 24	Key management personnel	1 July 2014
AIP IFRS 13	Scope of paragraph 52 (portfolio exception)	1 July 2014
IAS 1	Disclosure initiative	1 January 2016
IAS 16 and IAS 38	Clarification of acceptable methods of depreciation and amortisation	1 January 2016
AIP IFRS 7	Applicability of the offsetting disclosures to condensed interim financial statements	1 January 2016
AIP IAS 19	Discount rate: Regional market issue	1 January 2016
AIP IAS 34	Disclosure of information 'elsewhere in the interim financial report'	1 January 2016
IFRS 15	Revenue from contracts with customers	1 January 2017
IFRS 9	Financial instruments	1 January 2018

6 Segmental reporting

The Board regularly reviews the SHG Group's performance and balance sheet position for its operations and receives financial information for the SHG Group as a whole. As a consequence the SHG Group has one reportable segment, which is Clinical Development. Segmental profit is measured at operating loss level, as shown on the face of the Income Statement. As there is only one reportable segment whose losses, expenses, assets, liabilities and cash flows are measured and reported on a basis consistent with the financial statements, no additional numerical disclosures are necessary.

Following completion of the Corporate Reorganisation, PTL is expected to form a single separate additional segment which will comprise all of PTL's results.

7 Expenses and auditor's remuneration

	Year ended 31 December 2012	Year ended 31 December 2013	Year ended 31 December 2014	6 months to 30 June 2014 (unaudited)	6 months to 30 June 2015
	£000	£000	£000	£000	£000
Loss for the period has been arrived at after charging:					
Research and development expenditure	(3,370)	(3,123)	(2,668)	(1,192)	(1,215)
Audit of these financial statements	41	46	51	—	14

8 Staff numbers and costs

The average number of persons employed by SHG (including directors) during the year, analysed by category, was as follows:

	Number of employees				
	Year ended 31 December 2012	Year ended 31 December 2013	Year ended 31 December 2014	6 months to 30 June 2014 (unaudited)	6 months to 30 June 2015
	£000	£000	£000	£000	£000
Clinical operations	7	9	8	8	6
Manufacturing	1	1	1	1	1
Finance and administration	5	5	5	5	5
	13	15	14	14	12

The aggregate payroll costs of these persons were as follows:

	Year ended 31 December 2012	Year ended 31 December 2013	Year ended 31 December 2014	6 months to 30 June 2014 (unaudited)	6 months to 30 June 2015
	£000	£000	£000	£000	£000
Wages and salaries	986	1,061	1,067	497	560
Share based payments (see note 25#)	500	172	179	82	93
Other employee benefits	9	9	13	6	51
	1,495	1,242	1,259	585	704

9 Directors' emoluments

	Year ended 31 December 2012	Year ended 31 December 2013	Year ended 31 December 2014	6 months to 30 June 2014 (unaudited)	6 months to 30 June 2015
	£000	£000	£000	£000	£000
Amounts paid to third parties in respect of directors' services	—	14	18	9	291

10 Finance income and expenses

	Year ended 31 December 2012	Year ended 31 December 2013	Year ended 31 December 2014	6 months to 30 June 2014 (unaudited)	6 months to 30 June 2015
	£000	£000	£000	£000	£000
Financial income					
Net gain on financial instruments designated as fair value through profit or loss	532	569	—	—	—
Net foreign exchange gain	118	22	206	360	1,890
	650	591	206	360	1,890
Financial expense					
Total interest expense on financial liabilities measured at amortised cost	(500)	(1,255)	(1,655)	(827)	(1,295)
Bank charges	(5)	(11)	(5)	(5)	(4)
	(505)	(1,266)	(1,660)	(832)	(1,299)

11 Loss per share

	Year ended 31 December 2012	Year ended 31 December 2013	Year ended 31 December 2014	6 months to 30 June 2014 (unaudited)	6 months to 30 June 2015
Loss for the period (£000)	(3,460)	(4,517)	(13,430)	(11,766)	(30,027)
Weighted average number of shares	50,654,378	50,654,378	50,654,378	50,654,378	50,654,378
Basic and diluted loss per share	(6.8p)	(8.9p)	(26.5p)	(23.2p)	(59.3p)

The diluted loss per share is identical to the basic loss per share in all periods, as potential dilutive shares are not treated as dilutive since they would reduce the loss per share.

12 Taxation

Recognised in the income statement:

	Year ended 31 December 2012	Year ended 31 December 2013	Year ended 31 December 2014	6 months to 30 June 2014 (unaudited)	6 months to 30 June 2015
	£000	£000	£000	£000	£000
Current income tax:					
Current income tax expense	—	—	—	—	—
Foreign income taxes	—	—	—	—	—
Tax expense/(credit) relating to prior year	—	—	—	—	—
Deferred tax:					
Relating to origination and reversal of temporary differences	—	—	—	—	—
Effect of changes in the tax rate	—	—	—	—	—
Total tax expense	—	—	—	—	—

Reconciliation of total tax expense:

	Year ended 31 December 2012	Year ended 31 December 2013	Year ended 31 December 2014	6 months to 30 June 2014 (unaudited)	6 months to 30 June 2015
	£000	£000	£000	£000	£000
Loss excluding taxation	(3,460)	(4,517)	(13,430)	(11,766)	(30,027)
Standard rate of corporation tax in the UK	24.5%	23.25%	21.5%	22%	20.5%
Tax using the UK corporation tax rate	(848)	(1,050)	(2,887)	(2,589)	(6,156)
Expenses not deductible for tax purposes	123	1	37	—	1
Effect of tax rates in foreign jurisdictions	314	746	1,856	1,664	3,820
Unrelieved tax losses	411	303	1,093	925	2,335
Utilised tax losses	—	—	(98)	—	—
Total tax expense	—	—	—	—	—

Unrecognised deferred tax assets

There is a potential deferred tax asset in respect of the unutilised tax losses, which has not been recognised due to the uncertainty of available future taxable profits.

	Year ended 31 December 2012	Year ended 31 December 2013	Year ended 31 December 2014	6 months to 30 June 2014 (unaudited)	6 months to 30 June 2015
	£000	£000	£000	£000	£000
Unutilised Swiss tax losses to carry forward	5,096	8,616	11,628	10,122	12,746
Potential deferred tax asset thereon	450	724	957	810	1,082
Unutilised UK tax losses to carry forward	3,693	3,743	3,254	3,499	4,472
Potential deferred tax asset thereon	776	749	651	700	894

13 Property, plant and equipment

	31 December 2012	31 December 2013	31 December 2014	30 June 2014 (unaudited)	30 June 2015
	£000	£000	£000	£000	£000
Cost					
Beginning balance	5	5	5	5	12
Additions	—	—	12	—	10
Disposals	—	—	(5)	—	—
Ending balance	5	5	12	5	22
Accumulated depreciation					
Beginning balance	—	—	—	—	—
Charge for the period	—	—	5	1	2
On disposals	—	—	(5)	—	—
Ending balance	—	—	—	1	2
Net book values	5	5	12	4	20

14 Intangible assets

	31 December 2012	31 December 2013	31 December 2014	30 June 2014 (unaudited)	30 June 2015
	£000	£000	£000	£000	£000
Cost					
Beginning balance	336	388	486	486	566
Additions during the year	52	98	80	40	84
Ending balance	388	486	566	526	650
Accumulated amortisation:					
Beginning balance	39	67	99	100	131
Amortisation during the year	28	32	31	—	25
Ending balance	67	99	130	100	156
Net book values	321	387	436	426	494

15 Other receivables

	31 December 2012	31 December 2013	31 December 2014	30 June 2014 (unaudited)	30 June 2015
	£000	£000	£000	£000	£000
Receivables	101	81	51	213	85
Prepayments	23	20	28	42	55
	124	101	79	255	140

16 Cash and cash equivalents

	31 December 2012	31 December 2013	31 December 2014	30 June 2014 (unaudited)	30 June 2015
	£000	£000	£000	£000	£000
Cash at bank and in hand	651	627	477	1,573	3,663
Restricted cash	3,353	923	—	—	—
	4,004	1,550	477	1,573	3,663

Restricted cash represents cash funding received from investors for the issuance of additional share capital. Under Swiss law shares can only be issued once the capital increase has been registered with the Swiss authorities. Where cash is received close to year end there is not sufficient time for the registration to go through prior to year end. As a result the cash is held in a restricted account in line with Swiss law until the shares are issued.

17 Trade and other payables

	31 December 2012	31 December 2013	31 December 2014	30 June 2014 (unaudited)	30 June 2015
	£000	£000	£000	£000	£000
Trade payables	301	266	419	349	493
Accruals	602	653	275	195	530
	903	919	694	544	1,023

18 Interest bearing loans and borrowings

	31 December 2012	31 December 2013	31 December 2014	30 June 2014 (unaudited)	30 June 2015
	£000	£000	£000	£000	£000
Convertible bonds	—	—	197	—	891
Shares classified as debt	4,843	7,093	8,258	7,632	12,107
Interest bearing loans and borrowings	4,843	7,093	8,455	7,632	12,998

Terms and debt repayment schedule

	Currency	Face value 2012	Carrying Amount 2012	Face value 2013	Carrying Amount 2013	Face value 2014	Carrying amount 2014
		£000	£000	£000	£000	£000	£000
Convertible bonds	Euro	—	—	—	—	500	197
Shares classified as debt	Euro	8,200	4,843	9,300	7,093	9,300	8,258

	Currency	Face value 30 June 2014	Carrying amount 30 June 2014	Face value 30 June 2015	Carrying amount 30 June 2015
		£000	£000	£000	£000
Convertible bonds	Euro	—	—	2,000	891
Shares classified as debt	Euro	9,300	7,632	14,200	12,107

The convertible bonds carry a nominal interest rate of 10% and mature in 2019.

The shares carry a nominal interest rate of 10% and mature in 2016.

Preference shares

At 31 December 2014, there were 22,703,716 preference shares in issue. Each share is convertible at the option of the preference shareholder into one ordinary share of SHG at any time. As conversion into ordinary shares is a deemed settlement, the preference shares are treated as a current liability. The preference shares carry a dividend of 10% per annum, compounded annually. The preference shares rank ahead of the common shares in the event of a liquidation. The preference shares can be redeemed for cash or other assets for the Preferred Amount (see below) on either a Deemed Liquidity Event to the extent permitted by law or by the 31 December 2016 if a Deemed Liquidity Event has not occurred by that date. A Deemed Liquidity Event is defined as any distribution of assets or dissolution, or voluntary liquidation, plus any share sale, asset sale (constituting the sale of all undertakings and assets/rights without limitation by way of licencing or sub leasing), IPO, public merger or redemption of the preference shares.

The Preferred Amount is made up of the Liquidation Preference Amount (which is 1.5 times the amount of funding raised) plus the preferred dividend amount but is only payable to the extent the Group has sufficient funds. This preferred amount has been included in the cash flows in arriving at the amortised cost liability.

The preference shareholder has a put option to provide financing to SHG up to a maximum amount of EUR 8 million. On exercise of the option, the preference shareholder provides the financing and in turn, receives Series A Preferred Shares. This option and the entitlement to the Liquidation Preference Amount were cancelled as part of the Corporate Reorganisation, pursuant to which the W. Health Replacement Option was granted.

Convertible loan

ITH issued a convertible loan for the face value of euro 2,000,000 in 4 equal tranches on:

- 24 December 2014
- 16 February 2015
- 13 March 2015
- 15 April 2015

The Convertible Loan accrues interest at a rate of 10% per annum and is not compounding.

The outstanding loan amount plus accrued interest is payable on either a Deemed Liquidity Event or at maturity Date (24 December 2019). In addition the Group has the ability to repay the Convertible Loan at any time.

The Convertible Loan can be converted into newly issued A Shares at either a Deemed Liquidity Event or on maturity, at the request of the convertible Loan note holder. Prior to a Deemed Liquidity Event, the Convertible Loan can be repaid at the election of ITH.

The Convertible Loan has been exchanged for shares in ITH as part of the corporate reorganisation in preparation for Admission. Those shares in ITH were then ultimately exchanged for Ordinary Shares, also as part of the corporate reorganisation.

19 Other financial liabilities

	31 December 2012	31 December 2013	31 December 2014	30 June 2014 (unaudited)	30 June 2015
	£000	£000	£000	£000	£000
Preference Share Derivatives	(1,871)	(1,312)	(9,895)	(11,129)	(36,960)
Convertible Loan Conversion Option	—	—	(194)	—	(1,768)

The preference share conversion options and the put option to provide additional financing are embedded derivatives. These are treated as embedded derivatives because the debt that can be converted is in a currency which is different to the financial currency of the entity. They have therefore been separated from the host Preference Share financial instrument. The fair value of the conversion option of the outstanding Preference Shares and the option to subscribe for additional preference Shares has been calculated using a Black-Scholes-Morton model for a European option.

The Convertible Loan conversion option is an embedded derivative. It has been separated from the host Convertible Loan financial instrument. The fair value of the conversion option on the outstanding convertible notes has been calculated using Black-Scholes-Merton model for an American option.

The valuation requires management to make certain assumptions about the model inputs, including forecast cash flows and volatility. In particular, estimates of company valuations at different points in time have had to be determined with reference to observable inputs including market interest rates and volatility index for similar listed companies. The ranges of estimates within the calculation can be reasonably assessed and are used in the management's estimate of fair value.

20 Fair value hierarchy

The SHG Group uses the following hierarchy for determining the disclosing the fair value of financial instruments by valuation technique:

Level 1: quoted (unadjusted) prices in active markets for identical assets or liabilities

Level 2: other techniques for which all inputs which have a significant effect on the recorded fair value are observable, either directly or indirectly;

Level 3: techniques which use inputs which have a significant effect on the recorder fair value that are not based on observable market data.

Other than the embedded derivatives included under 'Other Financial Liabilities', 'Cash at bank and in hand, Restricted cash, Other receivables, Trade and other payables, Other liabilities and Interest bearing loans and borrowings have fair values that approximates its carrying values.

The table below summarises the fair values of embedded derivatives according to the fair value hierarchy:

Asset/liabilities measured at fair value	**30 June 2015**	**Level 1**	**Level 2**	**Level 3**
	£000	**£000**	**£000**	**£000**
Convertible Loan Conversion Option	(1,768)	—	—	(1,768)
Preference Shares Option	(36,960)	—	—	(36,960)

Asset/liabilities measured at fair value	**30 June 2014 (unaudited)**	**Level 1**	**Level 2**	**Level 3**
	£000	**£000**	**£000**	**£000**
Preference Share Option	(11,129)	—	—	(11,129)

Asset/liabilities measured at fair value	**31 December 2014**	**Level 1**	**Level 2**	**Level 3**
	£000	**£000**	**£000**	**£000**
Convertible Loan Conversion Option	(194)	—	—	(194)
Preference Share Option	(9,895)	—	—	(9,895)

Asset/liabilities measured at fair value	**31 December 2013**	**Level 1**	**Level 2**	**Level 3**
	£000	**£000**	**£000**	**£000**
Preference Share Option	(1,312)	—	—	(1,312)

Asset/liabilities measured at fair value	**31 December 2012**	**Level 1**	**Level 2**	**Level 3**
	£000	**£000**	**£000**	**£000**
Preference Share Option	(1,871)	—	—	(1,871)

21 Significant unobservable inputs to valuations

The significant unobservable inputs used in the fair value measurement categories within Level 3 of the fair value hierarchy together with a quantitative sensitivity analysis are as shown below:

30 June 2015

	Valuation technique	Significant unobservable inputs	Range (Weighted average)	Sensitivity of the input to fair value
Convertible bonds	Black-Scholes-Merton Model	Volatility	16-18%	10% increase (decrease) in the volatility rate would result in increase (decrease) in fair value by approximately €150,000
Preference Shares Option	Black-Scholes-Merton Model	Volatility Firm value	16-17%	10% increase (decrease) in the volatility rate would result in increase (decrease) in fair value by approximately €8,360,000

30 June 2014 (unaudited)

	Valuation technique	Significant unobservable inputs	Range (Weighted average)	Sensitivity of the input to fair value
Preference Shares Option	Black-Scholes-Merton Model	Volatility Firm Value	38-39%	10% increase (decrease) in the volatility rate would result in increase (decrease) in fair value by approximately €5,280,000

31 December 2014

	Valuation technique	Significant unobservable inputs	Range (Weighted average)	Sensitivity of the input to fair value
Convertible bonds	Black-Scholes-Merton Model	Volatility	6%	10% increase (decrease) in the volatility rate would result in increase (decrease) in fair value by approximately €40,000
Preference Shares Option	Black-Scholes-Merton Model	Volatility Firm value	41-42%	10% increase (decrease) in the volatility rate would result in increase (decrease) in fair value by approximately €5,030,000

31 December 2013

	Valuation technique	Significant unobservable inputs	Range (Weighted average)	Sensitivity of the input to fair value
Preference Shares Option	Black-Scholes-Merton Model	Volatility Firm value	71-77%	10% increase (decrease) in the volatility rate would result in increase (decrease) in fair value by approximately €1,060,000

31 December 2012

	Valuation technique	Significant unobservable inputs	Range (Weighted average)	Sensitivity of the input to fair value
Preference Shares Option	Black-Scholes-Merton Model	Volatility Firm value	65-72%	10% increase (decrease) in the volatility rate would result in increase (decrease) in fair value by approximately €1,440,000

22 Risk management

The SHG Group is exposed to a variety of risks such as market risk, credit risk and liquidity risk. The SHG Group's principal financial instruments are

- loans and borrowings; and
- Other receivables, trade and other payables, and cash and short term deposits arising directly from operations.

This note provides further detail on financial risk management and includes quantitative information on the specific risks.

Categories of financial instruments

Convertible loans and preference shares in note 18 are recognised at amortised cost using the effective interest method. Both instruments have conversion and other options, which are treated as embedded derivatives and measured at fair value (see notes 19 – 21).

Fair values

The carrying values of financial assets and liabilities reasonably approximate their fair values.

Market risk

Market risk is the risk that the fair value of future cash flows of a financial instrument will fluctuate because of changes in market prices. Market risk comprises three types of risk: interest rate risk, currency risk and other prices risk, such as equity price risk.

As the interest rate on the SHG Group's borrowings is fixed, the group's exposure is primarily to the financial risks of changes in foreign currency exchange.

Sensitivity analysis

SHG recognises that movements in certain risk variables (such as foreign exchange rates) might affect the value of its loans and also the amounts recorded in its equity and its profit and loss for the period. Therefore SHG assessed the following risks:

Foreign currency risk

The following tables consider the impact of several changes to the spot £/euro exchange rates of +/- 5%. If these changes were to occur the tables below reflect the impact on profit before tax. Only the impact of changes in euro denominated balances have been considered as these are the most significant non-GBP denomination used by the SHG Group.

		Effect on loss before tax				
	Change in GBP vs. EUR rate	Year ended 31 December 2012	Year ended 31 December 2013	Year ended 31 December 2014	6 months to 30 June 2014 (unaudited)	6 months to 30 June 2015
EUR	+5.00%	(336)	(420)	(927)	(938)	(2,586)
	-5.00%	336	420	927	938	2,586

Liquidity risk

Cash flow is regularly monitored and the relevant subsidiaries are aware of their working capital commitments. The SHG Group reviews its long-term funding requirements in parallel with its long-term strategy, with an objective of aligning both in a timely manner.

The table below summarises the maturity profile of the SHG Group's undiscounted financial liabilities at 31 December 2012, 2013 and 2014, 30 June 2014 (unaudited) and 30 June 2015. It is assumed in these tables that redemption of the interest bearing borrowings takes place after 31 December 2016 and that the SHG Group has sufficient funds to make such payment lawfully. In practice the debt may also be settled by conversion into equity.

Liquidity Risks

	On demand	Less than one year	Between two and five years	More than five years	Total
	£000	£000	£000	£000	£000
Liquidity risk – 31 December 2012					
Financial liabilities					
Interest bearing loans and borrowings	—	—	17,107	—	17,107
Trade and other payables	—	301	—	—	301
	—	301	17,107	—	17,408

	On demand	Less than one year	Between two and five years	More than five years	Total
	£000	£000	£000	£000	£000
Liquidity risk – 31 December 2013					
Financial liabilities					
Interest bearing loans and borrowings	—	—	19,125	—	19,125
Trade and other payables	—	266	—	—	266
	—	266	19,125	—	19,391

	On demand	Less than one year	Between two and five years	More than five years	Total
	£000	£000	£000	£000	£000
Liquidity risk – 31 December 2014					
Financial liabilities					
Interest bearing loans and borrowings	—	—	19,875	—	19,875
Trade and other payables	—	419	—	—	419
	—	419	19,875	—	20,294

	On demand	Less than one year	Between two and five years	More than five years	Total
	£000	£000	£000	£000	£000
Liquidity risk – 30 June 2014 (unaudited)					
Financial liabilities					
Interest bearing loans and borrowings	—	—	19,125	—	19,125
Trade and other payables	—	349	—	—	349
	—	349	19,125	—	19,474

	On demand	Less than one year	Between two and five years	More than five years	Total
	£000	£000	£000	£000	£000
Liquidity risk – 30 June 2015					
Financial liabilities					
Interest bearing loans and borrowings	—	—	22,092	—	22,092
Trade and other payables	—	493	—	—	493
	—	493	22,092	—	22,585

Credit risk

Credit risk is the risk that a counter party will not meet its obligations under a financial instrument leading to a financial loss. The SHG Group is exposed to credit risk from its financing activities primarily in relation to its deposits with banks and financial institutions.

Financial instruments and cash deposits

Credit risk from balances with banks and financial institutions is managed by depositing with reputable financial institutions, from which management believes loss to be remote. The SHG Group's maximum exposure to credit risk for the components of the statement of financial position is the carrying amounts cash at bank and in hand.

23 Called up share capital

	31 December 2012	31 December 2013	31 December 2014	30 June 2014 (unaudited)	30 June 2015
	£000	£000	£000	£000	£000
Allotted, called up and fully paid					
51 million ordinary shares at CHF0.01 each	365	365	365	365	365

24 SHG Group structure and acquisition details

The SHG Group's equity interest was as follows:

During the year ended 31 December 2012 and 31 December 2013:

Group company	Ownership	Country of incorporation
Iron Therapeutics Holdings AG	91.40%	Switzerland
Iron Therapeutics (Switzerland) AG*	91.40%	Switzerland
Iron Therapeutics (UK) Ltd.*	91.40%	United Kingdom
Iron Therapeutics (US) Corp.*	91.40%	United States of America

* SHG holds an indirect ownership through Iron Therapeutics Holdings, AG.

During the year ended 31 December 2014:

Group company	Ownership	Country of incorporation
Iron Therapeutics Holdings AG	83.53%	Switzerland
Iron Therapeutics (Switzerland) AG*	83.53%	Switzerland
Iron Therapeutics (UK) Ltd.*	83.53%	United Kingdom
Iron Therapeutics (US) Corp.*	83.53%	United States of America

*SHG holds an indirect ownership through Iron Therapeutics Holdings, AG.

During the 6 months ended 30 June 2014 (unaudited):

Group company	Ownership	Country of incorporation
Iron Therapeutics Holdings AG	83.53%	Switzerland
Iron Therapeutics (Switzerland) AG*	83.53%	Switzerland
Iron Therapeutics (UK) Ltd.*	83.53%	United Kingdom
Iron Therapeutics (US) Corp.*	83.53%	United States of America

* SHG holds an indirect ownership through Iron Therapeutics Holdings, AG.

During the 6 months ended 30 June 2015:

Group company	Ownership	Country of incorporation
Iron Therapeutics Holdings AG	83.53%	Switzerland
Iron Therapeutics (Switzerland) AG*	83.53%	Switzerland
Iron Therapeutics (UK) Ltd.*	83.53%	United Kingdom
Iron Therapeutics (US) Corp.*	83.53%	United States of America

* SHG holds an indirect ownership through Iron Therapeutics Holdings, AG.

SHG holds investments in four entities, all of which have been classified as subsidiaries. Iron Therapeutics Holdings AG has a minority shareholder who own less than 20% of the group. The other subsidiary entities are then held 100% by ITH. Therefore Shield Holdings AG has control over ITH and the rest of the entities in the SHG Group.

Non-Controlling Interests

The following table summarises the information relating to Iron Therapeutics Holdings AG which is a subsidiary of SHG with a material Non-Controlling Interest, before intra-group eliminations.

£'000	31 December 2012	31 December 2013	31 December 2014	30 June 2014 (unaudited)	30 June 2015
NCI percentage	8.6%	8.6%	16.47%	16.47%	16.47%
Non-current assets	388	456	501	492	562
Current assets	2,008	1,905	1,585	4,284	2,414
Non-current liabilities	(3,203)	(6,701)	(7,514)	(7,041)	(9,931)
Current liabilities	(19)	(20)	(137)	(29)	(116)
Net assets (100%)	(826)	(4,360)	(5,565)	(2,294)	(7,071)
Carrying amount of NCI	*1,075*	*747*	*1,746*	*2,039*	*1,330*
Revenue	—	—	—	—	—
Loss	(1,245)	(3,582)	(3,393)	(33)	(1,241)
OCI	(5)	43	256	175	(2)
Total comprehensive income	(1,250)	(3,539)	(3,137)	142	(1,243)
Cash flows from operating activities	(600)	79	(1,818)	(631)	(747)
Cash flows from investing activities	(51)	(99)	(87)	(77)	(58)
Cash flows from financing activities	—	—	2,165	1,968	499
Net increase/(decrease) in cash and cash equivalents	(651)	(20)	260	1,260	(306)

25 Share based payments

The SHG Group grants rights to the parent entity's equity instruments to certain employees and non-employees, which are accounted for as equity-settled in the consolidated financial statements.

SHG Group EMI Share Option Plan

SHG Group operates a share option scheme for certain employees of Iron Therapeutics (UK) Ltd. The scheme, which is an Enterprise Management Incentives (EMI) Scheme, is intended to attract retain and incentivise participants to higher standards of performance and encourage greatest dedication and loyalty by enabling the group to give recognition to past contributions and services, as well as motivating participants to contribute to the long-terms prosperity of the group.

The total expense recognised for share based payments, in relation to the SHG EMI Share Option Plan, in the company's financial statements during the year was £179,130.

The terms and conditions of grants are as follows:

Grant date	Method of settlement accounting	Number of instruments	Vesting conditions	Contractual life of options
November 2011	Equity	2,110,172	1/3 on grant date. 1/3 on 1st anniversary of employment 1/3 on 2nd anniversary of employment.	November 2021
February 2012	Equity	275,000	Subject to achievement of non-market based performance conditions, 1/3 on 31 December 2015, 1/3 on 31 December 2016 and 1/3 on 31 December 2017.	February 2022
May 2013	Equity	1,250,000	Subject to achievement of non-market based performance conditions, 1/3 on 31 December 2015, 1/3 on 31 December 2016 and 1/3 on 31 December 2017.	May 2023
May 2013	Equity	40,000	All vest immediately.	May 2023
October 2013	Equity	25,000	1/3 on 30 April 2014, 1/3 on 31 October 2014 and 1/3 on 31 October 2015.	October 2023
October 2013	Equity	25,000	1/3 on 30 April 2014, 1/3 on 30 April 2015 and 1/3 on 31 April 2016.	October 2023
February 2014	Equity	25,000	1/3 on 1 September 2014, 1/3 on 1 September 2015 and 1/3 on 1 September 2016.	February 2024
August 2014	Equity	75,000	1/3 on 1 January 2015, 2/3 on 31 December 2015	August 2024
March 2015	Equity	377,010	1/3 on 31 December 2015, 1/3 on 31 December 2016, 1/3 on 31 December 2017	March 2025

The number and weighed average exercise price of share options are as follows:

	Year ended 31 December 2012 Number of options	Year ended 31 December 2013 Number of options	Year ended 31 December 2014 Number of options	6 months to 30 June 2014 (unaudited) Number of options	6 months to 30 June 2015 Number of options
Outstanding at the beginning of the year	2,110,172	1,261,726	1,475,000	1,475,000	1,570,000
Granted during the year	275,000	1,340,000	100,000	100,000	377,010
Forfeited during the year	(100,000)	(91,667)	(5,000)	—	—
Exercised during the year	(1,023,446)	(1,035,059)	—	—	—
Outstanding at the end of the year	1,261,726	1,475,000	1,570,000	1,575,000	1,947,010
Exercisable at the end of the year	500,003	116,666	205,000	205,000	205,000

The options outstanding at year end have an exercise price of £0.00 per share and weighted average contractual life of 9.34 years.

The fair value of services received in return for share options granted are measured by reference to the fair value of share options granted. The fair value of the services received is measured using a Black-Scholes valuation model measurement inputs and assumptions are as follows:

	March 2015	August 2014	February 2014	October 2013	May 2013	February 2012	November 2011
Weighted average share price	£0.40	£0.40	£0.40	£0.40	£0.40	£0.40	£0.40
Exercise price	£0.00	£0.00	£0.00	£0.00	£0.00	£0.00	£0.00
Expected volatility	70.00%	70.00%	70.00%	70.00%	70.00%	70.00%	70.00%
Expected option life	Nil	Nil	Nil	Nil	Nil	Nil	Nil
Expected dividends	Nil	Nil	Nil	Nil	Nil	Nil	Nil
Risk-free interest rate (based on UK government boards)	3.50%	3.50%	3.50%	3.50%	3.50%	3.50%	3.50%
Fair value at measurement date	£0.40	£0.40	£0.40	£0.40	£0.40	£0.40	£0.40

The expected volatility is based on the historical volatility of quoted companies in a similar market environment.

There are no market conditions associated with the share options grants.

All unexercised share options have corresponding shares that are held in trust by a third party.

SHG Group Other Share-based Payments

SHG Group has other equity-settled share-based payment agreements for services received by non-employees which are summarised as follows:

Grant date	Method of settlement accounting	Number of instruments	Vesting conditions	Contractual life of options
January 2011	Equity	75,656	All vests immediately	January 2021
May 2011*	Equity	189,237	All vests immediately	May 2021
May 2011	Equity	10,000	All vests immediately	May 2021
November 2011	Equity	25,000	All vests immediately	November 2021
January 2012*	Equity	36,960	All vests immediately	January 2022
May 2013	Equity	600,000	1/2 vests in 1 May 2013, 1/4 vests in 1 May 2014, 1/4 vests in 1 May 2015	May 2023
September 2013	Equity	175,788	All vests immediately	September 2023
January 2014	Equity	17,000	All vests immediately	January 2024
February 2015	Equity	52,596	All vests immediately	February 2025

* Pertains to equity-settled share-based payments to suppliers and contractors which have a fair value of £79,600.

The total expense recognised for share based payments, in relation to the SHG Other Share-based payments in the company's financial statements during the year was £1,602,632.

The number and weighed average exercise process of share options are as follows:

	Year ended 31 December 2012 Number of options	Year ended 31 December 2013 Number of options	Year ended 31 December 2014 Number of options	6 months to 30 June 2014 (unaudited) Number of options	6 months to 30 June 2015 Number of options
Outstanding at the beginning of the year	1,419,293	386,040	562,642	562,642	516,901
Granted during the year	36,960	227,455	27,000	17,000	72,595
Exercised during the year	(986,921)	(50,853)	—	—	—
Forfeited during the year	(83,292)	—	(72,741)	(72,741)	—
Outstanding at the end of the year	386,040	562,642	516,901	506,901	589,496
Exercisable at the end of the year	360,072	561,714	516,901	505,973	570,171

The fair value of services received for May 2011 and January 2012 share option issuances have been measured at the fair value of services received. The fair value of services received for all other share option issuances are measured by reference to the fair value of share options granted as the fair value of services could not be determined. The expense in relation to these share options is not material.

	February 2015	January 2014	September 2013	May 2013	November 2011	May 2011	January 2011
Weighted average share price	£0.40	£0.40	£0.40	£0.40	£0.40	£0.40	£0.40
Exercise price	£0.00	£0.00	£0.00	£0.00	£0.00	£0.00	£0.00
Expected volatility	70.00%	70.00%	70.00%	70.00%	70.00%	70.00%	70.00%
Expected option life	2.5 years	2.5 years	2.5 years	2.5 years	4.5 years	2.5 years	4.5 years
Expected dividends	Nil	Nil	Nil	Nil	Nil	Nil	Nil
Risk-free interest rate (based on UK government bonds)	3.50%	3.50%	3.50%	3.50%	3.50%	3.50%	3.50%
Fair value at measurement date	£0.40	£0.40	£0.40	£0.41	£0.40	£0.41	£0.40

The expected volatility is based on the historical volatility of quoted companies in a similar market environment.

There are no market conditions associated with the share options grants.

All unexercised share options have corresponding shares that are held in trust by a third party.

26 Related party transactions

SHG Group trades with Phosphate Therapeutics Limited, a company related by virtue of its linked key management personnel.

During the following periods the SHG Group's trading with PTL constituted:

	Year ended 31 December 2012	Year ended 31 December 2013	Year ended 31 December 2014	6 months to 30 June 2014 (unaudited)	6 months to 30 June 2015
	£000	£000	£000	£000	£000
Management services provided	203	244	244	124	120
Amounts due from related parties	24	50	45	115	26

Income from related parties relates to management services provided. These services were made at arm's length and on normal commercial trading terms.

The amounts outstanding are unsecured and are settled in cash with a 30-day credit period.

Key management compensation information is as follows:

	Year ended 31 December 2012	Year ended 31 December 2013	Year ended 31 December 2014	6 months to 30 June 2014 (unaudited)	6 months to 30 June 2015
	£000	£000	£000	£000	£000
Wages and salaries	765	861	866	410	410
Share based payments	403	172	145	73	92
Other employee benefits	6	7	9	4	—
	1,174	1,040	1,020	487	502

27 Capital commitments

SHG had no material capital commitments at the end of any of the financial periods.

28 Capital management policy

The primary objective of the SHG Group's capital management is to ensure that it has the capital required to operate and grow the business at a reasonable cost of capital without incurring undue financial risks. The SHG Board periodically reviews its capital structure to ensure it meets changing business needs. The SHG Group defines its capital as its share capital, share premium account, and retained earnings. In addition, the SHG directors consider the management of debt to be an important element in controlling the capital structure of the SHG Group. The SHG Group may carry significant levels of long- term debt to fund operations and working capital requirements. There have been changes to the capital requirements each year as SHG is a pre-revenue development company which has required regular suitable levels of capital injections to fund development. As mentioned above the SHG Board periodically monitor the capital structure of the SHG Group. The table below details the net capital structure at the relevant balance sheet dates.

	Year ended 31 December 2012	Year ended 31 December 2013	Year ended 31 December 2014	6 months to 30 June 2014 (unaudited)	6 months to 30 June 2015
	£000	£000	£000	£000	£000
Cash and cash equivalents	4,004	1,550	477	1,573	3,663
Loans and borrowings	(4,843)	(7,093)	(8,455)	(7,632)	(12,998)
	(839)	(5,543)	(7,978)	(6,059)	(9,335)

29 Subsequent events

Since 30 June 2015 a series of transactions have been entered into in preparation for the admission of the Company to the London Stock Exchange. In particular:

- SHG has a newly formed parent company, Shield Therapeutics plc. The acquisition was by share for share exchange and there has been no significant change in the ultimate shareholders prior to Admission.
- Iron Therapeutics (US) Corp. was struck off on 30 September 2015.
- SHG entered into an agreement, subject to Admission whereby, *inter alia*, the right to the Preferred Amount on the Series A preference shares is replaced by an option to subscribe for Ordinary Shares.

PART 6

HISTORICAL FINANCIAL INFORMATION FOR PHOSPHATE THERAPEUTICS

Section A: Accountant's report on consolidated historical information on PTL

The Directors
Shield Therapeutics plc
Northern Design Centre
Studio 6, 3rd Floor
Baltic Business Quarter
Gateshead Quays
NE8 3DF

12 February 2016

Ladies and Gentlemen

Shield Therapeutics plc – Phosphate Therapeutics Limited

We report on the financial information set out on pages 121 to 140 for the three years and six months ended 30 June 2015. This financial information has been prepared for inclusion in the Admission Document dated 12 February 2016 of Shield Therapeutics plc on the basis of the accounting policies set out in note 2. This report is required by Paragraph (a) of Schedule Two of the AIM Rules for Companies and is given for the purpose of complying with that paragraph and for no other purpose. We have not audited or reviewed the financial information for the six months ended 30 June 2014 which has been included for comparative purposes only, and accordingly do not express an opinion thereon.

Responsibilities

The Directors of Shield Therapeutics PLC are responsible for preparing the financial information on the basis of preparation set out in note 2 to the financial information and in accordance with International Financial Reporting Standards as adopted by the European Union.

It is our responsibility to form an opinion on the financial information and to report our opinion to you.

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

Basis of opinion

We conducted our work in accordance with Standards for Investment Reporting issued by the Auditing Practices Board in the United Kingdom. Our work included an assessment of evidence relevant to the amounts and disclosures in the financial information. It also included an assessment of the significant estimates and judgments made by those responsible for the preparation of the financial information and whether the accounting policies are appropriate to the entity's circumstances, consistently applied and adequately disclosed.

We planned and performed our work so as to obtain all the information and explanations 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 on financial information

In our opinion, the financial information gives, for the purposes of the Admission Document dated 12 February 2016, a true and fair view of the state of affairs of Phosphate Therapeutics Limited as at 31 December 2012, 2013 and 2014 and 30 June 2015 and of its losses, comprehensive income, cash flows and changes in equity for the three years and six months ended 30 June 2015 in accordance with the basis of preparation set out in note 2 and in accordance with International Financial Reporting Standards as adopted by the European Union.

Declaration

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

Yours faithfully

KPMG LLP

Section B: Historical financial information

Income statement

	Note	Year ended 31 December 2012	Year ended 31 December 2013	Year ended 31 December 2014	6 months to 30 June 2014 (unaudited)	6 months to 30 June 2015
		£000	£000	£000	£000	£000
Research and development expenditure		(513)	(1,647)	(2,810)	(1,245)	(1,718)
Administrative expenses		(203)	(106)	(207)	(67)	(339)
Operating loss	*5-8*	(716)	(1,753)	(3,017)	(1,312)	(2,057)
Financial income	*9*	11	4	—	—	27
Financial expense	*9*	(680)	(767)	(1,700)	(718)	(1,043)
Loss before tax		(1,385)	(2,516)	(4,717)	(2,030)	(3,073)
Taxation	*11*	19	286	(280)	—	—
Loss for the period		(1,366)	(2,230)	(4,997)	(2,030)	(3,073)
Basic and diluted loss per share	*10*	(£1.74)	(£2.83)	(£6.35)	(£2.58)	(£3.91)

All activities relate to continuing operations.

Statement of other comprehensive income

	Year ended 31 December 2012	Year ended 31 December 2013	Year ended 31 December 2014	6 months to 30 June 2014 (unaudited)	6 months to 30 June 2015
	£000	£000	£000	£000	£000
Loss for the period	(1,366)	(2,230)	(4,997)	(2,030)	(3,073)

Balance sheet

	Note	Year ended 31 December 2012	Year ended 31 December 2013	Year ended 31 December 2014	6 months to 30 June 2014 (unaudited)	6 months to 30 June 2015
		£000	£000	£000	£000	£000
Non-current assets						
Intangible assets	*12*	806	865	846	842	833
		806	865	846	842	833
Current assets						
Trade and other receivables	*13*	244	166	206	60	61
Other financial assets	*14*	—	—	1,563	—	—
Cash and cash equivalents	*15*	2,445	1,331	6	315	767
Tax receivable		19	306	—	306	—
		2,708	1,803	1,775	681	828
Total assets		3,514	2,668	2,621	1,523	1,661
Current liabilities						
Interest bearing loans and borrowings	*16*	(4,702)	(5,612)	(10,353)	(6,317)	(12,477)
Trade and other payables	17	(177)	(651)	(860)	(831)	(849)
Total liabilities		(4,879)	(6,263)	(11,213)	(7,148)	(13,326)
Net liabilities		(1,365)	(3,595)	(8,592)	(5,625)	(11,665)
Equity						
Share capital	*18*	1	1	1	1	1
Retained earnings		(1,366)	(3,596)	(8,593)	(5,626)	(11,666)
Total equity		(1,365)	(3,595)	(8,592)	(5,625)	(11,665)

Statement of changes in equity

	Share Capital	Retained Earnings	Total
	£000	£000	£000
Balance at 1 January 2012	1	—	1
Total comprehensive income for the period			
Profit or loss	—	(1,366)	(1,366)
Other comprehensive income	—	—	—
Total comprehensive income for the period	—	(1,366)	(1,366)
Balance at 31 December 2012	1	(1,366)	(1,365)
Balance at 1 January 2013	1	(1,366)	(1,365)
Total comprehensive income for the period			
Profit or loss	—	(2,230)	(2,230)
Other comprehensive income	—	—	—
Total comprehensive income for the period	—	(2,230)	(2,230)
Balance at 31 December 2013	1	(3,596)	(3,595)
Balance at 1 January 2014	1	(3,596)	(3,595)
Total comprehensive income for the period			
Profit or loss	—	(4,997)	(4,997)
Other comprehensive income	—	—	—
Total comprehensive income for the period	—	(4,997)	(4,997)
Balance at 31 December 2014	1	(8,593)	(8,592)

	Share Capital	Retained Earnings	Total
	£000	£000	£000
Balance at 1 January 2014	1	(3,596)	(3,595)
Total comprehensive income for the period			
Profit or loss	—	(2,030)	(2,030)
Other comprehensive income	—	—	—
Total comprehensive income for the period	—	(2,030)	(2,030)
Balance at 30 June 2014	1	(5,626)	(5,625)
Balance at 1 January 2015	1	(8,593)	(8,592)
Total comprehensive income for the period			
Profit or loss	—	(3,073)	(3,073)
Other comprehensive income	—	—	—
Total comprehensive income for the period	—	(3,073)	(3,073)
Balance at 30 June 2015	1	(11,666)	(11,665)

Cash Flow Statement

	Year ended 31 December 2012	Year ended 31 December 2013	Year ended 31 December 2014	6 months to 30 June 2014 (unaudited)	6 months to 30 June 2015
	£000	£000	£000	£000	£000
Cash flows from operating activities					
Loss for the period	(1,366)	(2,230)	(4,997)	(2,030)	(3,073)
Adjustments for:					
Depreciation, amortisation and impairment	—	—	63	31	31
Financial income	(11)	(4)	—	—	(27)
Financial expense	680	767	1,700	718	1,043
Taxation	(19)	(286)	280	—	—
	(716)	(1,753)	(2,954)	(1,281)	(2,026)
(Increase)/decrease in trade and other receivables	(244)	78	(40)	106	145
Increase/(decrease) in trade and other payables	177	474	209	180	(11)
	(783)	(1,201)	(2,785)	(995)	(1,892)
Tax received	—	—	26	—	—
Net cash from operating activities	(783)	(1,201)	(2,759)	(995)	(1,892)
Cash flows from investing activities					
Acquisitions of intangible assets	(806)	(59)	(44)	(8)	(18)
Amounts placed on deposit	—	—	(1,563)	—	—
Proceeds from disposal of investments	—	—	—	—	1,563
Net cash from investing activities	(806)	(59)	(1,607)	(8)	1,545
Cash flows from financing activities					
Proceeds from issue of preference share capital	4,024	—	3,332	—	1,059
Net cash generated by financing activities	4,024	—	3,332	—	1,059
Net increase/(decrease) in cash and cash equivalents	2,435	(1,260)	(1,034)	(1,003)	712
Effects of exchange rates on cash and cash equivalents	9	146	(291)	(13)	49
Cash and cash equivalents at the start of the period	1	2,445	1,331	1,331	6
Cash and cash equivalents at the end of the period	2,445	1,331	6	315	767

Notes
(forming part of the financial statements)

1 General information

Phosphate Therapeutics Limited ("PTL") is a company incorporated and domiciled in the UK.

It is engaged in the development of clinical state pharmaceutics to treat unmet medical needs.

2 Accounting policies

As detailed in paragraph 2 of Part 10 (*Additional Information*) of this Admission Document, in preparation for Admission the Group undertook a corporate reorganisation that will result in the Company, Shield Therapeutics plc, becoming the ultimate holding company of the Group. The corporate reorganisation steps comprise, amongst other things, the Company acquiring the entire issued share capital of SHG and, conditional upon Admission, the entire issued share capital of PTL. Whilst the Company is the legal acquirer, for accounting purposes the financial statements of the Company will be a continuation of SHG.

The financial information is presented on the basis of the accounting policies and practices of SHG as will be applied in the first published financial statements following Admission. It has not been prepared on the basis that the Corporate Reorganisation has completed. This Part 5 (*Historical financial information for Shield Holdings*) of the Admission Document includes information on the SHG Group and Part 6 (*Historical financial information for Phosphate Therapeutics*) of this Admission Document includes information on Phosphate Therapeutics Limited.

The financial information has been prepared for the purposes of the Admission Document in accordance with the requirements of Paragraph (a) of Schedule Two of the AIM Rules for Companies and in accordance with IFRS as adopted by the EU (EU-IFRS) and this basis of preparation, including the significant accounting policies, is set out below.

The directors of SHG are responsible for the preparation of this financial information.

The consolidated company financial statements have been prepared and approved by the directors in accordance with International Financial Reporting Standards as adopted by the EU ("**Adopted IFRSs**").

The accounting policies set out below have, unless otherwise stated, been applied consistently to all periods presented in these financial statements.

The financial statements are prepared on the historical cost basis except that the following assets and liabilities are stated at their fair value: derivative financial instruments and financial instruments classified as fair value through the profit or loss or as available-for-sale.

The functional currency of PTL is GBP. The financial statements are presented in GBP and all values are rounded to the nearest thousand (£000), except where otherwise indicated.

Going concern

PTL funds the development of its products and meets its day to day working capital requirements from cash reserves and shareholder funding in the form of equity and preference shares and shareholder loans. As more fully described in notes 16 and 19, whilst elements of shareholder funding have historically been treated as debt, the terms have been designed to ensure that any cash payments of interest or capital would only fall due when the company has sufficient funds. As explained in note 22, PTL has entered into an agreement with the shareholders that, conditional upon Admission, all of the shareholder debt, including any accrued interest, will be replaced with Ordinary Shares. As a result PTL would be debt free at the time of Admission.

As at 30 June 2015 PTL had cash resources of £767,000.

The Directors have prepared cash flow forecasts for a period that exceeds 12 months from the date of authorisation of these financial statements. These forecasts include estimates of both the costs and timing of the successful commercialisation of PTL's products. The Directors, taking into account the potential impact of delays and/ or cost overruns in those forecasts, are confident that the Placing would raise sufficient funds to bring PTL's products to a stage where they can generate significant revenues.

In the preparation of this Historical Financial Information, the Directors have assumed that the Placing will be completed as described elsewhere in this Admission Document. On the assumption of a successful completion of the Placing, the Directors are confident that PTL will have sufficient

resources to meet cash requirements for at least the 12 months following the date of approval of this report and accordingly have adopted the going concern basis in the preparation of this Historical Financial Information.

Foreign currency

Transactions in foreign currencies are translated to PTL's functional currencies at the foreign exchange rate ruling at the date of the transaction. Monetary assets and liabilities denominated in foreign currencies at the balance sheet date are retranslated to the functional currency at the foreign exchange rate ruling at that date. Foreign exchange differences arising on translation are recognised in the income statement. Non-monetary assets and liabilities that are measured in terms of historical cost in a foreign currency are translated using the exchange rate at the date of the transaction. Non-monetary assets and liabilities denominated in foreign currencies that are stated at fair value are retranslated to the functional currency at foreign exchange rates ruling at the dates the fair value was determined.

Classification of financial instruments issued by PTL

Following the adoption of IAS 32, financial instruments issued by PTL are treated as equity only to the extent that they meet the following two conditions:

(a) they include no contractual obligations upon the company to deliver cash or other financial assets or to exchange financial assets or financial liabilities with another party under conditions that are potentially unfavourable to the company; and

(b) where the instrument will or may be settled in the company's own equity instruments, it is either a non-derivative that includes no obligation to deliver a variable number of the company's own equity instruments or is a derivative that will be settled by the company's exchanging a fixed amount of cash or other financial assets for a fixed number of its own equity instruments.

To the extent that this definition is not met, the proceeds of issue are classified as a financial liability. Where the instrument so classified takes the legal form of the company's own shares, the amounts presented in these financial statements for called up share capital and share premium account exclude amounts in relation to those shares.

Where a financial instrument that contains both equity and financial liability components exists these components are separated and accounted for individually under the above policy.

Non-derivative financial instruments

Non-derivative financial instruments comprise investments in equity and debt securities, trade and other receivables, cash and cash equivalents, loans and borrowings, and trade and other payables.

Trade and other receivables

Trade and other receivables are recognised initially at fair value. Subsequent to initial recognition they are measured at amortised cost using the effective interest method, less any impairment losses.

Trade and other payables

Trade and other payables are recognised initially at fair value. Subsequent to initial recognition they are measured at amortised cost using the effective interest method.

Cash and cash equivalents

Cash and cash equivalents comprise cash balances and call deposits.

Investments in debt and equity securities

Investments are stated at amortised cost less impairment. Financial instruments held for trading are stated at fair value, with any resultant gain or loss recognised in profit or loss.

Other investments in debt and equity securities held by PTL are classified as being available-for-sale and are stated at fair value, with any resultant gain or loss being recognised directly in equity (in the fair value reserve), except for impairment losses and, in the case of monetary items such as debt securities, foreign exchange gains and losses. When these investments are derecognised, the cumulative gain or loss previously recognised directly in equity is recognised in profit or loss. Where these investments are interest-bearing, interest calculated using the effective interest method is recognised in profit or loss.

Interest-bearing loans and borrowings

Interest-bearing loans and borrowings are recognised initially at fair value less attributable transaction costs. Subsequent to initial recognition, interest-bearing borrowings are stated at amortised cost using the effective interest method, less any impairment losses.

Derivative financial instruments and hedging

Derivative financial instruments

Derivative financial instruments are recognised at fair value. The gain or loss on remeasurement to fair value is recognised immediately in profit or loss.

Intangible assets

Research and development

PTL's activities are still considered to be in the research phase and therefore all related expenditure has been recognised as an expense in the income statement.

As there has been no expenditure on development activities, there has been no capitalisation of research and development costs.

Expenditure in relation to patents registration and renewal of current patents are capitalised and recorded as intangible assets. Registration costs are continually incurred as PTL registers these patents in different countries. Intangible assets are stated at cost less accumulated amortisation and less accumulated impairment losses.

Amortisation

Amortisation is charged to the income statement on a straight-line basis over the estimated useful lives of the patents. Patent assets are amortised from the date they are available for use. The estimated useful lives are as follows:

- patents and licences over life of patent/licence, 15 years

Expenses

Financing income and expenses

Financing expenses comprise interest payable, finance charges on shares classified as liabilities and net foreign exchange losses that are recognised in the income statement (see foreign currency accounting policy). Financing income comprise interest receivable on funds invested, dividend income, and net foreign exchange gains.

Interest income and interest payable is recognised in profit or loss as it accrues, using the effective interest method. Dividend income is recognised in the income statement on the date the entity's right to receive payments is established. Foreign currency gains and losses are reported on a net basis.

Taxation

Tax on the profit or loss for the year comprises current and deferred tax. Tax is recognised in the income statement except to the extent that it relates to items recognised directly in equity, in which case it is recognised in equity.

Current tax is the expected tax payable or receivable on the taxable income or loss for the year, using tax rates enacted or substantively enacted at the balance sheet date, and any adjustment to tax payable in respect of previous years.

A deferred tax asset is recognised only to the extent that it is probable that future taxable profits will be available against which the temporary difference can be utilised.

3 Critical accounting judgements and key sources of estimation uncertainty

In the application of the company's accounting policies, which are described in Note 1, management is required to make judgements, estimates and assumptions about the carrying amounts of assets and liabilities that are not readily apparent from other sources.

The estimates and underlying assumptions are reviewed on an ongoing basis. Revisions to accounting estimates are recognised in the period in which the estimate is revised if the revision affects only that period or in the period of the revision and future periods if the revision affects both current and future periods.

Capitalisation of development costs

Capitalisation of development costs requires analysis of the technical feasibility and commercial viability of the project concerned. Capitalisation of the costs will only be made where there is evidence that an economic benefit will flow to the company. To date no development costs have been capitalised and all costs have been expenses to the income statement as research and development expenditure.

Deferred tax assets

Estimates of future profitability are required for the decision whether or not to create a deferred tax asset. To date no deferred tax assets have been recognised.

Intangible assets valuation

Determining whether intangible assets are impaired requires an estimation of the values in use of the cash generating unit to which the intangible asset has been allocated. This value in use calculation requires an estimation of the future cash flows expected to arise from the cash generating unit and a suitable discount rate in order to calculate the present value. To date no impairment of intangible assets has been recognised.

4 New standards and interpretations

The following new standard was effective from the period beginning 1 January 2014:

IFRS 13 Fair Value Measurement

IFRS 13 establishes a single source of guidance under IFRS for all fair value measurements. IFRS 13 does not change when an entity is required to use fair value, but rather provides guidance on how to measure fair value under IFRS. IFRS 13 defines fair value as an exit price. As a result of the guidance in IFRS 13, PTL has included the fair value measurement policy in Note 2 above.

The following standards and interpretations have an effective date after the date of these financial statements. PTL has not early adopted them and plans to adopt them from the effective dates. Their adoption is not anticipated to have material effect on the financial statements.

Standard or interpretation	Title	Effective for accounting periods beginning on or after
AIP IFRS 2	Definition of vesting conditions	1 July 2014
AIP IAS 24	Key management personnel	1 July 2014
AIP IFRS 13	Scope of paragraph 52 (portfolio exception)	1 July 2014
IAS 1	Disclosure initiative	1 January 2016
IAS 16 and IAS 38	Clarification of acceptable methods of depreciation and amortisation	1 January 2016
AIP IFRS 7	Applicability of the offsetting disclosures to condensed interim financial statements	1 January 2016
AIP IAS 19	Discount rate: Regional market issue	1 January 2016
AIP IAS 34	Disclosure of information 'elsewhere in the interim financial report'	1 January 2016
IFRS 15	Revenue from contracts with customers	1 January 2017
IFRS 9	Financial instruments	1 January 2018

5 Segmental reporting

The PTL Board regularly reviews PTL's performance and balance sheet position for its operations and receives financial information for PTL as a whole. As a consequence PTL has one reportable segment, which is Clinical Development. Segmental profit is measured at operating loss level, as shown on the face of the Income Statement. As there is only one reportable segment whose losses, expenses, assets, liabilities and cash flows are measured and reported on a basis consistent with the financial statements, no additional numerical disclosures are necessary.

6 Expenses and auditor's remuneration

	Year ended 31 December 2012	Year ended 31 December 2013	Year ended 31 December 2014	6 months to 30 June 2014 (unaudited)	6 months to 30 June 2015
	£000	£000	£000	£000	£000
Loss for the period has been arrived at after charging:					
Research and development expenditure	513	1,647	2,810	1,245	1,718
Audit of these financial statements	4	5	6	—	4
Tax services	2	4	—	—	—

7 Staff numbers and costs

Other than directors, whose emoluments are described below, the company had no other employees.

8 Directors emoluments

	Year ended 31 December 2012	Year ended 31 December 2013	Year ended 31 December 2014	6 months to 30 June 2014 (unaudited)	6 months to 30 June 2015
	£000	£000	£000	£000	£000
Amounts paid to third parties in respect of directors' services	21	28	35	19	17

9 Finance income and expenses

	Year ended 31 December 2012	Year ended 31 December 2013	Year ended 31 December 2014	6 months to 30 June 2014 (unaudited)	6 months to 30 June 2015
	£000	£000	£000	£000	£000
Finance income					
Net foreign exchange gain	11	4	—	—	27
Total finance income	11	4	—	—	27

	Year ended 31 December 2012	Year ended 31 December 2013	Year ended 31 December 2014	6 months to 30 June 2014 (unaudited)	6 months to 30 June 2015
	£000	£000	£000	£000	£000
Finance expense					
Total interest expenses on financial liabilities measured at amortised cost	680	767	1,410	705	1,043
Net foreign exchange loss	—	—	290	13	—
Total finance expense	680	767	1,700	718	1,043

10 Loss per share

	Year ended 31 December 2012	Year ended 31 December 2013	Year ended 31 December 2014	6 months to 30 June 2014 (unaudited)	6 months to 30 June 2015
Loss for the period (£000)	(1,366)	(2,230)	(4,997)	(2,030)	(3,073)
Weighted average number of shares	786,787	786,787	786,787	786,787	786,787
Basic and diluted loss per share	(£1.74)	(£2.83)	(£6.35)	(£2.58)	(£3.91)

The diluted loss per share is identical to the basic loss per share in all periods, as potential dilutive shares are not treated as dilutive since they would reduce the loss per share.

11 Taxation

	Year ended 31 December 2012	Year ended 31 December 2013	Year ended 31 December 2014	6 months to 30 June 2014 (unaudited)	6 months to 30 June 2015
	£000	£000	£000	£000	£000
Recognised in the income statement:					
Current tax					
– current year	(19)	(286)	—	—	—
– adjustments for prior periods	—	—	280	—	—
Deferred tax expense	—	—	—	—	—
Tax (credit)/charge for the period	(19)	(286)	280	—	—

The tax credit assessed for the period relates entirely to R&D tax credit relief.

Reconciliation of total tax expense:

	Year ended 31 December 2012	Year ended 31 December 2013	Year ended 31 December 2014	6 months to 30 June 2014 (unaudited)	6 months to 30 June 2015
	£000	£000	£000	£000	£000
Loss for the period	(1,366)	(2,230)	(4,997)	(2,030)	(3,073)
Total tax (credit)/expense	(19)	(286)	280	—	—
Loss excluding taxation	(1,385)	(2,516)	(4,717)	(2,030)	(3,073)
Tax using the UK corporation tax rate of 20%	(277)	(503)	(943)	(406)	(615)
Research and development tax credit	(19)	(286)	—	—	—
Non deductible expenses	—	164	393	106	195
Current year losses for which no deferred tax asset was recognised	277	339	550	300	420
Under provided in prior years	—	—	280	—	—
Tax (credit)/charge for the period	(19)	(286)	280	—	—

The company has £7,251,000 of trading losses carried forward at 30 June 2015 for which no deferred tax asset has been recognised due to the uncertainty of available of future taxable profits.

A reduction in the UK corporation tax rate from 24% to 23% (effective 1 April 2013) was substantively enacted on 3 July 2012. Further reductions to 21% (effective from 1 April 2014) and 20% (effective from 1 April 2015) were substantively enacted on 2 July 2013. In the Budget on 8 July 2015, the Chancellor announced additional planned reductions to 18% by 2020. This will reduce the company's future current tax charge accordingly.

12 Intangible assets

	Licence	Total
	£000	£000
Cost		
Balance at 1 January 2012	—	—
Additions	806	806
At 31 December 2012	806	806
Balance at 1 January 2013	806	806
Additions	59	59
Balance at 31 December 2013	865	865
Balance at 1 January 2014	865	865
Additions	44	44
Balance 31 December 2014	909	909
Balance at 1 January 2015	909	909
Additions	18	18
Balance at 30 June 2015	927	927
Amortisation		
Balance at 31 December 2012, 31 December 2013 and 1 January 2014	—	—
Charge for the year	63	63
At 31 December 2014	63	63
Balance at 1 January 2015	63	63
Charge for the period	31	31
Balance at 30 June 2015	94	94
Net book value		
At 31 December 2012	806	806
At 31 December 2013	865	865
At 31 December 2014	846	846
At 30 June 2015	833	833
At 30 June 2014	842	842

Intangible assets relates to a licence to exploit rights and know how from the Medical Research Council (MRC).

13 Trade and other receivables

	Year ended 31 December 2012	Year ended 31 December 2013	Year ended 31 December 2014	6 months to 30 June 2014 (unaudited)	6 months to 30 June 2015
	£000	£000	£000	£000	£000
VAT	244	166	49	60	61
Other receivables	—	—	155	—	—
Prepayments	—	—	2	—	—
	244	166	206	60	61

All amounts due as shown above are short-term.

14 Other financial assets

	Year ended 31 December 2012	Year ended 31 December 2013	Year ended 31 December 2014	6 months to 30 June 2014 (unaudited)	6 months to 30 June 2015
	£000	£000	£000	£000	£000
Current					
Held to maturity financial assets	—	—	1,563	—	—

15 Cash and cash equivalents

	Year ended 31 December 2012	Year ended 31 December 2013	Year ended 31 December 2014	6 months to 30 June 2014 (unaudited)	6 months to 30 June 2015
	£000	£000	£000	£000	£000
Cash and cash equivalents	2,445	1,331	6	315	767

16 Other interest-bearing loans and borrowings

	31 December 2012	31 December 2013	31 December 2014	30 June 2014 (unaudited)	30 June 2015
	£000	£000	£000	£000	£000
Current liabilities					
Shares classified as debt	4,702	5,612	10,353	6,317	12,477

Terms and debt repayment schedule

	Face value 2012	Carrying amount 2012	Face value 2013	Carrying amount 2013	Face value 2014	Carrying amount 2014
	£000	£000	£000	£000	£000	£000
Shares classified as debt	4,165	4,702	4,165	5,612	7,497	10,353

	Face value 30 June 2014	Carrying amount 30 June 2014	Face value 30 June 2015	Carrying amount 30 June 2015
	£000	£000	£000	£000
Shares classified as debt	4,165	6,317	8,576	12,477

Interest is charged at 10% on the Series A preference shares and, to the extent that a deemed liquidity event has not occurred by 31 December 2016, the shares can be redeemed, at the option of the holder, in the following twelve months.

17 Trade and other payables

	Year ended 31 December 2012	Year ended 31 December 2013	Year ended 31 December 2014	6 months to 30 June 2014 (unaudited)	6 months to 30 June 2015
	£000	£000	£000	£000	£000
Trade payables	137	389	645	431	508
Accrued expenses and deferred income	40	262	215	400	341
	177	651	860	831	849

18 Capital and reserves

	10% cumulative redeemable preference shares				
	Year ended 31 December 2012	Year ended 31 December 2013	Year ended 31 December 2014	6 months to 30 June 2014 (unaudited)	6 months to 30 June 2015
On issue at 1 January	—	1,063,226	1,063,226	1,063,226	2,398,178
Issued for cash	1,063,226	—	1,334,952	—	364,078
On issue at period end fully paid	1,063,226	1,063,226	2,398,178	1,063,226	2,762,256

	Ordinary shares				
	Year ended 31 December 2012	Year ended 31 December 2013	Year ended 31 December 2014	6 months to 30 June 2014 (unaudited)	6 months to 30 June 2015
On issue at 1 January	786,787	786,787	786,787	786,787	786,787
Issued for cash	—	—	—	—	—
On issue at period end fully paid	786,787	786,787	786,787	786,787	786,787

	Year ended 31 December 2012	Year ended 31 December 2013	Year ended 31 December 2014	6 months to 30 June 2014 (unaudited)	6 months to 30 June 2015
	£000	£000	£000	£000	£000
Allotted, called up and fully paid					
Ordinary shares of 0.1p each	1	1	1	1	1
10% cumulative redeemable preference shares of 0.1p each	1	1	2	1	3
	2	2	3	2	4

	Year ended 31 December 2012	Year ended 31 December 2013	Year ended 31 December 2014	6 months to 30 June 2014 (unaudited)	6 months to 30 June 2015
	£000	£000	£000	£000	£000
Shares classified as liabilities	1	1	2	1	3
Shares classified in shareholders' funds	1	1	1	1	1
	2	2	3	2	4

The shares classified as liabilities have a nominal value of £2,000 and a carrying value of £10,353,000 at 31 December 2014 (see note 16).

Each share is convertible at the option of the preference shareholder into one ordinary share at any time. As conversion into ordinary shares is a deemed settlement, the preference shares are treated as a current liability. The preference shares carry a dividend of 10% per annum, compounded annually. The preference shares rank ahead of the ordinary shares in the event of a liquidation. The preference shares can be redeemed for cash or other assets for the Preferred Amount (see below) on either a Deemed Liquidity Event to the extent permitted by law or by the 31 December 2016 if a Deemed Liquidity Event has not occurred by that date. A Deemed Liquidity Event is defined as any distribution of assets or dissolution, or voluntary liquidation, plus any share sale, asset sale (constituting the sale of all undertakings and assets/rights without limitation by way of licencing or sub leasing), IPO, public merger or redemption of the preference shares.

The preference shares have a conversion option where a fixed number of shares can be issued by the entity and therefore have been accounted for as a compound financial instrument in accordance with IAS 32. The equity component of this compound financial instrument is not material and therefore no equity component has been recognised.

The Preferred Amount is made up of the Liquidation Preference Amount (which is 1.5 times the amount of funding raised) plus the preferred dividend amount, but is only payable to the extent the company has sufficient funds. This preferred amount has been included in the cash flows in arriving at the amortised lost liability.

The following shares were issued in the financial periods:

	Year ended 31 December 2012	Year ended 31 December 2013	Year ended 31 December 2014	6 months to 30 June 2014 (unaudited)	6 months to 30 June 2015
Preference shares (number)	1,063,226	—	1,334,952	—	364,078
Preference share capital (£)	£1,063	—	£1,335	—	£364
Subscription amounts settled in cash (£)	£4,024,000	—	£3,332,000	—	£1,059,000

19 Financial instruments

PTL's activities expose it to a variety of financial risks: credit risk, liquidity risk and market risk (including foreign currency risk and interest rate risk. This note address each of these matters in turn, and also gives details of financial assets and liabilities with a carrying value that is materially different to their fair value and the company's capital management objectives.

Fair values

The carrying values of financial assets and liabilities reasonably approximate their fair values.

a) Credit risk

Credit risk is the risk of financial loss to PTL if a customer or counterparty to a financial instrument fails to meet its contractual obligations, and arises principally from PTL's receivables from customers.

The carrying amount of the company's financial assets is as follows:

	Year ended 31 December 2012	Year ended 31 December 2013	Year ended 31 December 2014	6 months to 30 June 2014 (unaudited)	6 months to 30 June 2015
	£000	£000	£000	£000	£000
Trade and other receivables	244	166	204	60	61
Short term investments	—	—	1,563	—	—
Cash and cash equivalents	2,445	1,331	6	315	767
	2,689	1,497	1,773	375	828

No amounts are past due in the current or prior year so the risk arises principally in respect of the counterparty to the company's fixed term deposits. The deposit counterparty has a Moody's credit rating of A2 in line with the company's treasury policy.

b) Liquidity risk

Liquidity risk is the risk that the company will not be able to access the necessary funds to finance its operations.

The carrying amount of the company's financial liabilities is as follows:

	Year ended 31 December 2012	Year ended 31 December 2013	Year ended 31 December 2014	6 months to 30 June 2014 (unaudited)	6 months to 30 June 2015
	£000	£000	£000	£000	£000
Trade payables	137	389	645	431	508
Shares classified as debt	4,702	5,612	10,353	6,317	12,477
	4,839	6,001	10,998	6,748	12,985

The company finances its operations through the issue of equity and non-equity shares. The company manages its liquidity risk by monitoring existing and committed funding against forecast requirements (with particular reference to non-discretionary expenditure). The following are the contractual maturities of financial liabilities, including estimated interest payments. It is assumed in these tables that redemption of the interest bearing borrowings takes place after 31 December 2016 and that the company has sufficient funds to make such payment lawfully. In practise the debt may also be settled by conversion into equity.

	31 December 2014				
	Carrying amount	Contractual cashflows	1 year or less	1 to 2 years	2 to 5 years
	£000	£000	£000	£000	£000
Trade payables	645	645	645	—	—
Shares classified as debt	10,353	15,234	—	—	15,234
	10,998	15,879	645	—	15,234

	31 December 2013				
	Carrying amount	Contractual cashflows	1 year or less	1 to 2 years	2 to 5 years
	£000	£000	£000	£000	£000
Trade payables	389	389	389	—	—
Shares classified as debt	5,612	9,122	—	—	9,122
	6,001	9,511	389	—	9,122

	31 December 2012				
	Carrying amount	Contractual cashflows	1 year or less	1 to 2 years	2 to 5 years
	£000	£000	£000	£000	£000
Trade payables	137	137	137	—	—
Shares classified as debt	4,702	9,122	—	—	9,122
	4,839	9,259	137	—	9,122

	30 June 2015				
	Carrying amount	Contractual cashflows	1 year or less	1 to 2 years	2 to 5 years
	£000	£000	£000	£000	£000
Trade payables	508	508	508	—	—
Shares classified as debt	12,477	17,120	—	8,254	8,866
	12,985	17,628	508	8,254	8,866

	30 June 2014 (unaudited)				
	Carrying amount	Contractual cashflows	1 year or less	1 to 2 years	2 to 5 years
	£000	£000	£000	£000	£000
Trade payables	431	431	431	—	—
Shares classified as debt	6,317	9,122	—	—	9,122
	6,748	9,553	431	—	9,122

As explained in note 18 the shares classified as debt can be redeemed, at the Investor's notice, at any time after 31 December 2016. Redemption would be in 50% tranches spread over a period of up to 24 months. Whilst this would be an unavoidable liability for the company, and is therefore treated as debt, redemption can only be made if the company has sufficient distributable reserves to make the redemption payment.

c) Market risk – Foreign currency risk

Foreign currency risk reflects the company's exposure to fluctuations in foreign exchange rates on its financial assets and liabilities.

The company's exposure to foreign currency risk on financial assets and liabilities is as follows:

	Euro				
	Year ended 31 December 2012	Year ended 31 December 2013	Year ended 31 December 2014	6 months to 30 June 2014 (unaudited)	6 months to 30 June 2015
	£000	£000	£000	£000	£000
Short term investments	—	—	1,563	—	—
Cash and cash equivalents	2,322	1,105	—	34	352
Total assets	2,322	1,105	1,563	34	352
Trade and other payables	—	(531)	(590)	(1)	(39)
Total liabilities	—	(531)	(590)	(1)	(39)
Net exposure	2,322	574	973	33	313

	US Dollar				
	Year ended 31 December 2012	Year ended 31 December 2013	Year ended 31 December 2014	6 months to 30 June 2014 (unaudited)	6 months to 30 June 2015
	£000	£000	£000	£000	£000
Trade and other receivables	—	166	155	—	—
Short term investments	—	—	—	—	—
Cash and cash equivalents	—	139	2	121	126
Total assets	—	305	157	121	126
Trade payables	—	—	(115)	(140)	(320)
Total liabilities	—	—	(115)	(140)	(320)
Net exposure	—	305	42	(19)	(194)

The company manages foreign currency exposure by matching expected currency outflows with inflows of the same currency to the extent possible. The company would consider hedging instruments if there was considered to be a significant mismatch but this has not proven necessary to date.

The following table considers the impact of several changes to the spot £/euro and US Dollar exchange rates of +/- 1%, assuming all other variables remain constant. If these changes were to occur the tables below reflect the impact on loss before tax.

	Year ended 31 December 2012	Year ended 31 December 2013	Year ended 31 December 2014	6 months to 30 June 2014 (unaudited)	6 months to 30 June 2015
	£000	£000	£000	£000	£000
1% increase in Euro	(23)	(6)	(10)	—	(3)
1% increase in US Dollar	—	(3)	—	—	(2)

d) Market risk – Interest rate risk

Interest rate risk reflects the company's exposure to fluctuations in interest rates. The interest rate profile of the company's interest bearing financial instruments is as follows:

As the company has no variable rate financial instruments a 1% change in interest rates would have no impact on profit or loss and equity in the current or prior year.

e) Capital management

The company does not yet have any significant recurring revenues and finances its operations through the issue of shares and management of working capital. At this stage in its development, capital is measured as the sum of cash and cash equivalents and fixed term deposits less short term debt and was as follows at the various periods:

	Year ended 31 December 2012	Year ended 31 December 2013	Year ended 31 December 2014	6 months to 30 June 2014 (unaudited)	6 months to 30 June 2015
	£000	£000	£000	£000	£000
Cash and cash equivalents	2,445	1,331	6	315	767
Fixed term deposits	—	—	1,563	—	—
Loans and borrowings	(4,702)	(5,612)	(10,353)	(6,317)	(12,477)
	(2,257)	(4,281)	(8,784)	(6,002)	(11,710)

There are no minimum capital requirements imposed by regulatory or other bodies but the level of capital does determine the level of expenditure to which the company can commit.

20 Capital commitments

The company had no material capital commitments at the end of the financial periods.

21 Related party transactions

Phosphate Therapeutics Limited trades with Iron Therapeutics UK Limited a company related by virtue of its linked key management personnel.

During the period PTL's trading with Iron Therapeutics constituted:

	Year ended 31 December 2012	Year ended 31 December 2013	Year ended 31 December 2014	6 months to 30 June 2014 (unaudited)	6 months to 30 June 2015
	£000	£000	£000	£000	£000
Purchase of goods and services	203	244	244	124	120
Amounts owed to related parties	24	50	45	115	26

Purchase of goods and services from related parties comprise management services. These were made at arm's length and on normal commercial trading terms.

The amounts outstanding are unsecured and will be settled in cash within a 30 day credit period.

22 Subsequent events

Since 30 June 2015 a series of transactions have been entered into in preparation for the admission of the Company to the London Stock Exchange. In particular:

- PTL was agreed to be acquired by the Company, conditional upon Admission. The acquisition will be by way of share for share exchange.

23 Ultimate controlling party

The company's controlling shareholder is W Health LP part of Inventages Whealth Management Inc, one of the world's largest life sciences, nutrition and wellness focussed venture capital funds.

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STRATAGEM INTELLECTUAL PROPERTY MANAGEMENT LIMITED

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Baltic Business Quarter
Gateshead Quays
NE8 3DF

Liberum Capital Limited
Ropemaker Place
25 Ropemaker Street
London EC2Y 9LY

("**Nominated Adviser and Broker**")

12 February 2016

Dear Sirs

Re: PATENT AND TRADE MARK REPORT

We have prepared this report for the directors of Shield Therapeutics plc (the "**Company**") and the Nominated Adviser and Broker for inclusion in the admission document issued by the Company in connection with the admission of the Company's entire issued and to be issued ordinary share capital and Warrants to trading on AIM (the "**Admission Document**").

We declare that we are responsible for this report, which forms part of the Admission Document, and that we have taken all reasonable care to ensure that the information contained in this report is, to the best of our knowledge and belief, in accordance with the facts and contains no omission likely to affect its interpretation.

EXECUTIVE SUMMARY

The Company is an independent pharmaceutical company focused on the development of speciality medicines for significant unmet medical needs. The Company will hold two direct subsidiaries, being Shield Holdings AG and Phosphate Therapeutics Limited ("**PTL**"). Iron Therapeutics Holdings AG is a subsidiary of Shield Holdings AG and its key asset is FERACCRU®, an oral ferric iron-based therapy. FERACCRU offers an alternative oral-based therapy to intravenous iron. The main asset of PTL is PT20, an iron oxide composition which functions as a phosphate binder for the treatment of hyperphosphatemia. In this report,

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the "**Group**" means the Company and its subsidiaries and subsidiary undertakings, and, where the context requires it, its associated undertakings.

The Group is expecting to enter the market with FERACCRU in 2016 and a Marketing Authorisation Application (MAA) for the treatment of iron deficiency anaemia (IDA), initially in patients with inflammatory bowel disease (IBD), was accepted for review in December 2014 by the European Medicines Agency. This is expected by the Group to be approved in the first quarter of 2016. Once the MAA is granted, the Group can rely on 8 years of data exclusivity and a further 2 years of marketing exclusivity protection, preventing third parties from marketing FERACCRU in Europe during this period based on the Group's clinical trial data. In the US the Group can expect 3 years of exclusivity. Assuming FERACCRU is approved in 2016, the Group will have exclusivity for FERACCRU until 2026 in the EU. The Group expects to launch FERACCRU in Europe as a twice daily 30mg dose for the treatment of IDA initially in patients with IBD. In light of novel findings in the pharmacokinetic (PK) study conducted in subjects with iron deficiency (with or without anaemia) in the EU, the Group is considering an alternate enhanced dosing strategy in the US which is reflected in the patent strategy. These studies, in conjunction with an Orange Book listing of certain key US patents (explained in further detail in Appendix I), will support the regulatory approval of FERACCRU in the US for this dose.

The Group intends to sell FERACCRU in Europe, United States, Japan and Rest of the World. Manufacturing of FERACCRU will be carried out in Europe.

In May 2015, PT20 showed positive results in a Pharmacodynamic Evaluation of Adipate modified iron in subjects with Chronic kidney disease and Hyperphosphatemia who were dependent on dialysis (PEACH) study. This was a pivotal Phase 2b study.

In addition to data exclusivity, the Group has a number of patent and patent application families which cover the method of manufacture, polymorphs, formulation and dosing regimes of FERACCRU, together with patents covering alternative formulations and method of manufacture, providing protection for specific aspects of FERACCRU and its use. The Group is active in filing further applications surrounding the intended treatment regime and formulation of FERACCRU.

The scope of granted patent family P005 extends to FERACCRU produced by the claimed process, providing the Group with the right to prevent importation of FERACCRU produced by that process into the US and any validated European patent ("EP") territory. The Group intends to apply for patent term extension on both the European and US patents following grant of respective marketing authorisation, further extending protection by up to five years to 2028. New crystalline forms of FERACCRU are covered by patent application family P012 which if granted will provide key product protection to 2035. This family will be important in extending exclusivity beyond 2026 and will be Orange Book listed (explained in further detail in Appendix I). The intended dosing regimes are covered by patent application

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families P010 and P014 which if granted will prevent third parties from selling FERACCRU for use with the claimed dose. Patent application family P011 covers liquid compositions of FERACCRU and future formulations relevant for paediatric treatment. P007, P010 and P014 will also be Orange Book listed in addition to P012.

PTL has an exclusive licence from the Medical Research Council (MRC) to a granted patent family (PT20 Family P001) which protects the PT20 process of production, compositions produced by that process and medical use. The complexes (ligand-modified poly oxo-hydroxy metal ion complexes) of the invention have a broad range of medicinal applications and in view of this the exclusive licence is limited to the fields of phosphate binding for the treatment of renal diseases and/or intravenous iron for the treatment of iron deficiency anaemias. This patent family provides PTL with the right to prevent third parties from using PT20 produced by the claimed process according to the licensed field and from importing the PT20 complex into a territory where the process claim is granted and in force (such as the US and any validated EP territory), to expiry in 2028 (or August 2029 for the US patent).

PTL has also exclusively licensed from the MRC a second patent family (PT20 Family P002) which covers the specific medical use of ligand-modified poly oxo-hydroxy metal ion complexes in the treatment of hyperphosphatemia. This application has been granted in the US and is pending in Europe. This patent family provides PTL with valuable specific medical use protection for PT20 in its intended indication.

The following tables summarise the patent term of the key patent families for FERACCRU and PT20, including data and marketing exclusivity in Europe for FERACCRU (patent term expiry in the US may differ to the terms represented here - US expiry dates are provided later in the report):

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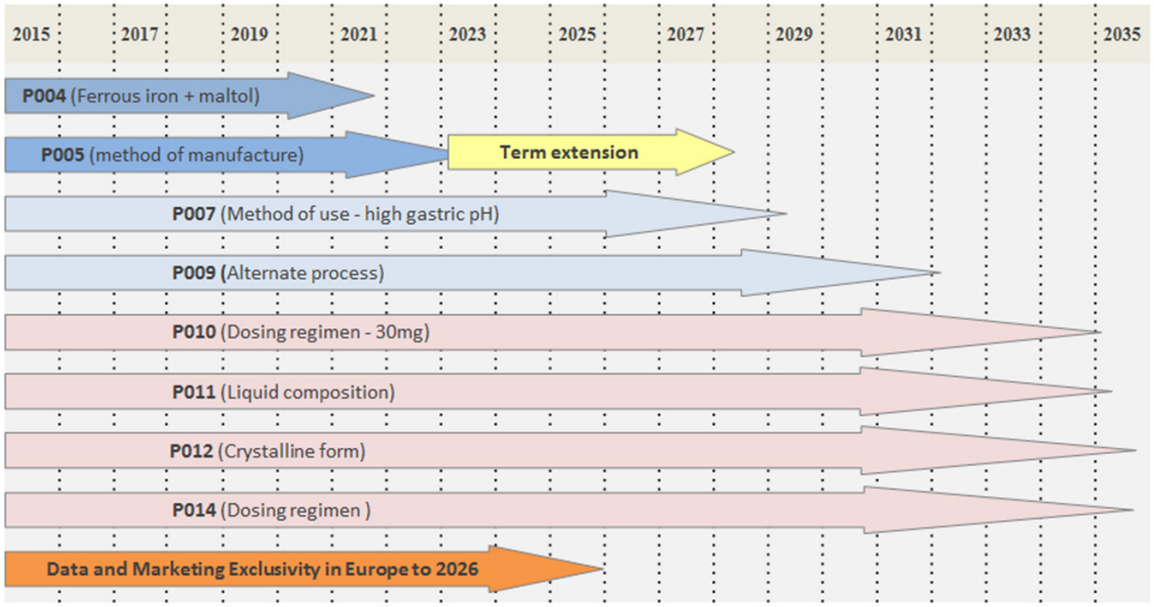
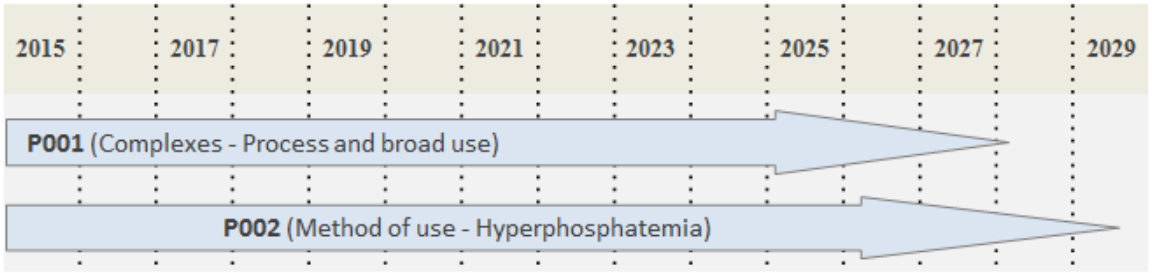
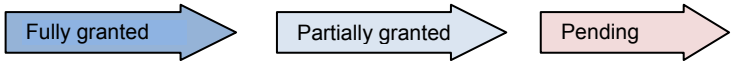
FERACCRU:



PT20:



Legend



All patent rights detailed in this report relating to FERACCRU are in the name of Iron Therapeutics Holdings AG. All patent rights detailed in this report relating to PT20 for the treatment of hyperphosphatemia have been exclusively licensed by PTL from the Medical Research Council (referred to in further detail in section 2 below).

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SCOPE OF REPORT

This patent and trade mark report relates to the patent and trade mark rights of the Group. Stratagem IPM Ltd has been commissioned to review the registered patent and trade mark rights owned by and licensed to the Group and to provide this report.

The contact details for Stratagem are as follows:

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Meridian Court
Comberton Road
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UK

Tel: +44 (0) 1223 550740
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The relevant attorney details are as follows:

Nicola Baker-Munton CPA, EPA
Abigail Woolhouse RTMA, ETMA

As Stratagem IPM Limited ("Stratagem"), we act as intellectual property advisors and patent and trade mark attorneys to the Group. The professional staff at Stratagem who act for the Group are UK Chartered Patent Attorneys and European Patent Attorneys, and UK Registered Trade Mark Attorneys and European Trade Mark Attorneys, who have the necessary technical specialism and are legally qualified to act for technology clients before the UK Intellectual Property Office (UKIPO), the European Patent Office (EPO) and the International Patent and Trade Mark Office. We also have expertise in areas of intellectual property such as designs, copyright and trade secrets.

Nicola Baker-Munton is the founder and Chief Executive Officer of Stratagem. She is a UK Chartered Patent Attorney and European Patent Attorney with a joint honours degree in biology and biochemistry. Nicola spent nine years as an industrial practitioner at the Wellcome Foundation Limited, and has been advising companies in the private sector for nineteen years. Nicola founded Stratagem in 1999.

Abigail Woolhouse joined Stratagem in 2005 and is a Registered Trade Mark Attorney and European Trade Mark Attorney. She began her career in private practice, moving to ICI in 1999 taking on responsibility for various trade mark portfolios within the ICI Group and management of the domain name portfolio. Since working for Stratagem, Abigail has

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provided strategic advice in the fields of trade marks, copyright, domain names and agreements to individuals, start-ups, SMEs and international companies Abigail has also been involved in the resolution of many Trade Mark disputes.

Stratagem has been engaged by the Company's subsidiaries since 2012 and has assisted in their intellectual property management and strategy.

For each patent family exclusively in-licensed or owned by the Company's subsidiaries, a paragraph has been written which summarises the invention and its commercial context. In addition to the summary table we have also summarised the overall status of each patent family. Opinions expressed in this summary are based on our best assessment of the relevant facts and information known to us, and represent our honest belief.

This report is not intended as a substitute for reviewing the publicly available prosecution files which, in the case of the European Patent Office and the US Patent & Trade Mark Office (USPTO), are available online. Reports from the Patent Co-operation Treaty (PCT) procedure are also available online from the World Intellectual Property Organisation (WIPO).

For exclusively in-licensed rights, the licences have not been reviewed by Stratagem. And as such the detail of these licences is not within the scope of this report. For in-licensed rights, the ownership has been checked at the USPTO and EPO, although original documents, such as contracts of employment of inventors, or previous assignments to the licensor, have not generally been sought. The correctness of the inventorship has also not been checked for any patent families prosecuted by Potter Clarkson LLP or Mewburn Ellis LLP.

THE GROUP'S PATENT FILING AND MAINTENANCE POLICY

The Group's IP strategy is to seek effective and comprehensive patent protection wherever possible. Stratagem is responsible for the prosecution of FERACCRU patent families P010 and P014 and for the handling and payment of all renewals for the FERACCRU portfolio. Potter Clarkson LLP are responsible for the prosecution of patent families P001, P002, P003, P004, P005, P007, P009, P011 and P012. Mewburn Ellis LLP is responsible for the prosecution and renewals for both P001 and P002 PT20 patent families.

In general, the Group's new applications are first filed at the UK Patent Office. An additional search is requested when the UK application is filed. Any prior art found by the UK Patent Office is reviewed by the patent firm responsible and the Group. Any relevant prior art is taken into consideration when deciding whether to file an international application and when finalising the scope of the claims of the international application.

The Group's policy is to draft initial patent applications as broadly as possible, with a series of gradually narrowing dependent claims directed to more specific forms (embodiments) of

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the invention. The aim is also to try and include claims that cover the composition to be sold (product claims) and how it is produced (method claims). In addition the Group aims to secure use claims that cover the particular aspects of how FERACCRU and / or PT20 will be used in treatment (e.g. dosage regimens).

International applications that claim priority from the original UK or US priority filing(s) are filed within a year as Patent Cooperation Treaty international applications. It is the Group's policy to pursue these applications as national phase applications in major territories, including at least the USA and Europe and consider filing more broadly depending on the commercial significance of the case. Any granted European patents would, typically, be validated in major European countries, for example, UK, France, Germany, Spain and Italy, with additional countries considered based on the commercial significance of the case and the importance of the market.

This report contains a summary description of the various inventions to which the Group has access via in-licensed patents, or for which the Group is seeking or has obtained patent protection. This description has been simplified to assist the reader.

This report also contains summaries of investigations conducted on behalf of the Group. The summaries should not be relied upon as an exhaustive description of the investigations and analysis performed, nor are they necessarily as detailed as reports provided to the Group.

REVIEW OF GROUP OWNED AND LICENSED PATENTS

1. FERACCRU / iron patent families

FERACCRU (also referred to as ST10, ferric maltol or ferric tri-maltol) is an iron-based therapy for the treatment of iron deficiency anaemia (IDA) and represents the Group's lead asset. FERACCRU is a complex of ferric iron (Fe^{3+}) and maltol (3-hydroxy-2-methyl-4-pyrone) and is an alternative treatment for patients who are intolerant of oral ferrous therapies.

The pending MAA (Marketing Authorisation Application) is supported by phase III clinical trial data in inflammatory bowel disease (IBD) patients, showing that FERACCRU delivered a mean increase in haemoglobin levels of 2.25g/dL in 12 weeks, clearly meeting the primary endpoint of haemoglobin change compared to placebo ($p<0.0001$).

The Group also intends to study FERACCRU for the treatment of iron deficiency anaemia (IDA) in pre-dialysis chronic kidney disease patients and data from this study will, together with existing data, support a New Drug Application (NDA) submission to the FDA in the USA.

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The Group owns an established patent portfolio comprising granted patents and applications relating to FERACCRU compositions, medical uses and methods of production. The portfolio also comprises patent families that do not relate directly to the Group's activities, but instead cover potential competitor products for the same market, for example ferrous iron compositions and ferric tri-maltol/carboxylic acid compositions.

1.1 Schedule for Family P005 - Method of forming Iron hydroxypyrone compounds

a. PCT Abstract
A method of forming an iron hydroxypyrone compound comprising reacting an iron salt of a carboxylic acid and a hydroxypyrone in an aqueous solution at a pH greater than 7.

b. Ownership
This patent family is in the name of Iron Therapeutics Holdings AG.

c. Inventors
Michael Arthur Stockham

d. Summary of Invention and Commercial Context
PCT/GB2003/01956 was filed on 7 May 2003 claiming priority from GB0211500.4 filed on 18 May 2002, and published as WO2003/097627 on 27 November 2003. The application entered the national phase in November 2005 in Canada, Europe, India and United States. The patents in this family will expire in May 2023 except the US patent which will expire in August 2023.

The invention relates to a method of forming an iron hydroxypyrone (of which maltol is an example of a hydroxypyrone) compound by reacting an iron salt of a carboxylic acid and a hydroxypyrone in an aqueous solution at a pH of greater than 7, wherein the aqueous solution comprises a base.

The granted main claim in Europe is as follows:

"A method of forming an iron hydroxypyrone compound comprising reacting an iron salt of a carboxylic acid and a hydroxypyrone in an aqueous solution at a pH greater than 7, wherein the aqueous solution comprises a base".

This family is currently the key granted protection for FERACCRU and provides broad comprehensive protection for the most efficient method of production of an iron hydroxypyrone. The method offers the advantage of an improved yield and purity over other manufacturing methods.

This family protects a method of manufacture of FERACCRU used by the Group and is of high commercial importance.

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The scope of the process claim extends to the product produced by that process, therefore this family provides the Group with a legal right to prevent third parties from importing iron hydroxypyrone produced by the claimed process into a validated EP territory, and ferric hydroxypyrone (in a 3:1 ratio of hydroxypyrone to ferric iron) produced by the claimed process into the US, where the iron hydroxypyrone or ferric hydroxypyrone is produced directly by that process.

Once the MA is obtained, a Supplementary Protection certificate (SPC) may be applied for in Europe potentially providing up to 5 years additional protection in respect of the product produced by the process. Term extension can also be obtained in the US (up to five years) following FDA approval.

e. Prosecution
A divisional application in India is pending.

f. Family P005- Patent Summary Table

Country	Filing date	Status	Application number	Publication number
Canada	07/05/2003	Granted	2483067	CA2483067
Europe (BE, CH, DE, ES, FR, UK, IE, IT, LI)	07/05/2003	Granted	03727643.3	EP1506183
India	07/05/2003	Granted	3267/DELNP/2004	IN248503
India divisional	07/05/2003	Pending	3600/DELNP/2011	-
United States	07/05/2003	Granted	10/514836	Patent No. US7459569
WO	07/05/2003	Gone National	PCT/GB03/01956	WO2003/097627

1. 2 Schedule for Family P012 - Crystalline Forms

a. Summary of Invention and Commercial Context
PCT/EP2015/074653 was filed on 23 October 2015 claiming priority from GB1419174.6 filed on 28 October 2014. The application will publish in April 2016 and national phase entry is due in April 2017.

The invention relates to new crystalline forms of ferric maltol.

This application is of high importance since it protects the form of ferric maltol to be sold and other polymorphic forms. If granted this family will provide key composition of matter protection for the product up to 2035.

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b. Abstract
Not yet published

c. Ownership
This patent family is in the name of Iron Therapeutics Holdings AG.

d Inventors
To be confirmed

e. Prosecution
Prosecution is awaited.

The Group intends to prosecute this application in additional countries as prosecution progresses.

f. Family P012- Patent Summary Table

Country	Filing date	Status	Application number	Publication number
UK	28/10/2014	Pending	1419174.6	-
WO	23/10/2015	Pending	PCT/EP2015/074653	-

1.3 Schedule for Family P011 - Composition

a. Summary of Invention and Commercial Context
PCT/GB2015/050711 was filed on 11 March 2015 claiming priority from GB1404390.5 filed on 12 March 2014, and published as WO2015/136282 on 17 September 2015. National phase entry is due in September 2016. If granted this patent family is expected to expire in March 2035.

The invention relates to compositions comprising iron hydroxypyrone in a liquid or liquid suspension formulation.

This patent application protects a liquid or liquid suspension formulation of FERACCRU and is relevant to the development of a paediatric formulation and other possible formulations in the future.

b. PCT Abstract
The invention provides a composition in the form of a liquid or liquid suspension, comprising an iron hydroxypyrone and a taste masking agent, and wherein the iron

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hydroxypyrone is present in the liquid or suspension in a molar concentration of at least -5 M (mol/L).

c. Ownership
This patent family is in the name of Iron Therapeutics Holdings AG.

d. Inventors
Michael Arthur Stockham

e. Prosecution
Prosecution is awaited.

The Group intends to prosecute this application in additional countries as prosecution progresses.

f. Family P011- Patent Summary Table

Country	Filing date	Status	Application number	Publication number
WO	11/03/2015	Pending	PCT/GB2015/050711	WO2015/136282

1.4 Schedule for Family P010 – Dosage Regimen of Ferric Trimaltol

a. PCT Abstract
The present invention relates to a dosage regimen of ST10 (ferric trimaltol) for the treatment of patients suffering from iron deficiency with or without anaemia. Specifically the invention relates to the treatment of patients with 30mg ST10 twice daily.

b. Ownership
This patent family is in the name of Iron Therapeutics Holdings AG.

c. Inventors
Carl Andrew Sterritt; Christian Schweiger; Julian David Howell.

d. Summary of Invention and Commercial Context
PCT/IB2015/050098 was filed on 6 January 2015 claiming priority from GB1400171.3 filed on 6 January 2014 and GB1418708.2 filed on 21 October 2014. The application published as WO2015/101971 on 9 July 2015. National phase entry is due in June 2016. If granted this patent family is expected to expire in January 2035.

The invention relates to a 30mg bid dosage regime for a new FERACCRU composition and covers the dose intended to be prescribed for sale in Europe.

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e. Prosecution

The International Search Report and Written Opinion issued in June 2015. Novelty of all the claims was acknowledged; however inventive step objections have been raised in view of prior art disclosing treatment of patients intolerant of ferrous iron with 30mg ferric trimaltol twice daily. The Group is considering generating further data to support this application.

Claim 1 as pending:

ST10 for use in the treatment or prevention of iron deficiency with or without anaemia wherein said ST10 is administered orally as a 30mg preparation on an empty stomach twice daily, wherein the percentage of ST10 is at least 60% of the combined weight of ST10 and excipients.

The Group intends to prosecute this application in additional countries as prosecution progresses.

f. Family P010- Patent Summary Table

Country	Filing date	Status	Application number	Publication number
WO	06/01/2015	Pending	PCT/IB2015/050098	WO2015/101971

1.5 Schedule for Family P014 – Dosage regimen

a. Summary of Invention and Commercial Context

PCT/IB2015/058115 was filed on 21 October 2015 claiming priority from GB1418710.8 filed on 21 October 2014. National phase entry is due in April 2017. If granted this patent family is expected to expire in October 2035.

The invention relates to a novel dosage regime for FERACCRU in the treatment of iron deficiency with or without anaemia.

This application protects a higher dosage regime which if granted will provide valuable additional protection preventing others from selling FERACCRU for use in the claimed range. The Group intends to prosecute this family in the US and, if granted, will be Orange Book listed meaning that a generic company has a legal obligation to notify the Group if it plans to make or sell FERACCRU which would arguably infringe the patent.

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b. Abstract
Not yet published

c. Ownership
This patent family is in the name of Iron Therapeutics Holdings AG.

d. Inventors
Nicholas Mallard; Carl Andrew Sterritt; Julian David Howell.

e. Prosecution
Prosecution is awaited.

The Group intends to prosecute this application in additional countries as prosecution progresses.

f. Family P014- Patent Summary Table

Country	Filing date	Status	Application number	Publication number
WO	21/10/2015	Pending	PCT/IB2015/058115	-

1.6 Schedule for Family P007 - Mono (iron hydroxypyrone) and combination (iron hydroxypyrone and GI inflammation inhibiting agents) compositions for anaemia or H. pylori infections

a. PCT Abstract
There is provided a composition or kit of parts comprising: one or more compounds capable of treating and/or preventing an inflammatory disease of the gastrointestinal tract: and an iron hydroxypyrone, for increasing the level of iron in a patient's bloodstream and/or treating and/or preventing anaemia such as iron deficiency anaemia. A composition comprising iron hydroxypyrone is also provided for administration to a subject: having or at risk of having achlorhydria; wherein the gastric pH of the subject is equal to or greater than about 4; or wherein the subject has an inflammatory disease of the gastrointestinal tract.

b. Ownership
This patent family is in the name of Iron Therapeutics Holdings AG.

c. Inventors
Michael Arthur Stockham

d. Summary of Invention and Commercial Context

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PCT/GB2009/001231 was filed on 14 May 2009 claiming priority from GB0808835.3 filed on 15 May 2008, and published as WO2009/138761 on 19th November 2009. The application entered the national phase in November 2010 in Australia, Canada, China, Europe, Hong Kong, India, Japan, Singapore and the United States. Any granted patents in this family will expire in May 2029.

The invention relates to a composition comprising a compound for treating an inflammatory disease of the GI tract and iron hydroxypyrone for the treatment of anaemia. The invention also relates to an iron hydroxypyrone composition for the treatment of anaemia in GI inflammatory conditions. If granted, the US patent will be Orange Book listed meaning that a generic company has a legal obligation to notify the Group if it plans to make or sell FERACCRU, the use of which would arguably infringe the patent.

e. Prosecution

Applications are currently pending in Canada, Europe, India, Japan (divisional), Singapore (divisional) and United States.

The main claim as pending in Europe is as follows:

"A composition for use in preventing and/or treating iron deficiency anaemia, comprising an iron hydroxypyrone for administration to a subject, wherein the gastric pH of the subject is equal to or greater than 4."

This claim, if granted, will provide the Group with the right to prevent others from using FERACCRU for the prevention or treatment of iron deficiency anaemia for any condition where the gastric pH is 4 or above and so may provide broad protection in this respect.

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f. Family P007- Patent Summary Table

Country	Filing date	Status	Application number	Publication number
Australia	14/05/2009	Granted	2009247762	AU2009247762
Canada	14/05/2009	Pending	2724172	CA2724172
China	14/05/2009	Granted	200980125291.4	CN102099042
Europe	14/05/2009	Pending	09746078.6	EP2303289
Hong Kong (CN)	17/10/2011	Granted	11111059.2	1156552
Hong Kong (EP)	03/10/2011	Pending	11110432.2	-
India	14/05/2009	Pending	4766/KOLNP/2010	IN04766KN2010
Japan	14/05/2009	Granted	2011-509003	JP2011520855
Japan divisional	14/05/2009	Pending	2014-237229	JP2015083572
Singapore	14/05/2009	Granted	201008312-9	SG166433
Singapore divisional	14/05/2009	Pending	201203891-5	SG182137
United States	14/05/2009	Allowed	12/992528	US2011/177172
WO	14/05/2009	Gone National	PCT/GB2009/001231	WO2009/138761

1.7 Schedule for Family P004 - Iron compositions including SIDEROMAL®

a. PCT Abstract

Compositions in solid form, such as powders, comprising a mixture of a ferrous salt and a hydroxypyrone may be used to increase the level of iron in a patient's bloodstream or to treat and/or prevent gastrointestinal infection.

b. Ownership

This patent family is in the name of Iron Therapeutics Holdings AG.

c. Inventors

Michael Arthur Stockham

d. Summary of Invention and Commercial Context

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PCT/GB2001/004052 filed on 10 September 2001 claiming priority from GB0022881 filed on 19 September 2000 and GB0107031 filed on 21 March 2001 and published as WO2002/024196 on 28 March 2002. The application entered the national phase in Canada, Europe and US in March 2003. The patents in this family will expire in September 2021, except the US patent which will expire in January 2022.

The invention relates to iron compositions comprising a mixture of a ferrous salt and a hydroxypyrone.

The granted main claim of EP1318804 is as follows:

"Pharmaceutical composition which is in the form of a solid or a suspension in liquid form and which comprises a ferrous salt and a hydroxypyrone together with a pharmaceutically acceptable diluent or carrier".

The claims are directed to ferrous iron in combination with a hydroxypyrone and so do not cover FERACCRU, therefore this family serves to deter competitors from the IDA market by protecting the less preferred alternative to ferric iron (which is branded by the Group as SIDEROMAL).

e. Prosecution
Prosecution completed in all territories.

f. Family P004 - Patent Summary Table

Country	Filing date	Status	Application number	Publication number
Canada	10/09/2001	Granted	2421410	CA2421410
Europe (BE, CH, DE, ES, FR, UK, IE, IT, LI)	10/09/2001	Granted	01967474.6	EP1318804
United States	10/09/2001	Granted	10/380751	Patent No. US7135196
WO	10/09/2001	Gone National	PCT/GB01/04052	WO2002/24196

1.8 Schedule for Family P001 - Iron Compounds, compositions, methods of making the same and compositions thereof

a. PCT Abstract
The invention relates to complexes comprising iron in the ferric state and a hydroxypyrone for use in the manufacture of a composition for use in medicine.

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b. Ownership
This patent family is in the name of Iron Therapeutics Holdings AG.

c. Inventors
Michael Arthur Stockham; Charles Robert Hider.

d. Summary of Invention and Commercial Context
This patent was filed on 10 June 1996 as international application PCT/GB96/01382 claiming priority from GB9511818.8 filed on 10 June 1995 and GB9517537.8 filed on 26 August 1995. The application published on 27 December 1996 as WO96/41627. In February 1998 the application entered the national phase in United States, Europe and South Africa.

The invention relates to the addition of a carboxylic acid to the iron:hydroxypyrone composition. The acid acts as a counter ion in solution, allowing a higher proportion of free Fe^{3+} in solution available for absorption.

The patent is granted in Europe and the United States and has lapsed in South Africa. The patents in this family expire in June 2016.

The granted European patent has a main claim as follows:

"An iron complex comprising iron in the ferric state and a hydroxypyrone ligand and characterised in that the iron and hydroxypyrone are provided in combination with a carboxylic acid as a counterion".

The Group does not use a FERACCRU formulation comprising a carboxylic acid and therefore this patent family is not relevant in protecting FERACCRU in its current or intended formulation, but prevents competitors from entering the same market with an alternative product.

e. Prosecution
Prosecution completed in all territories.

f. Family P001 - Patent Summary Table

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Country	Filing Date	Status	Application Number	Publication number
Europe (DE, ES, FR, UK, IT)	10/06/1996	Granted	96917578.5	EP0833627
US Divisional	10/06/1996	Granted	09/983656	US6635631
United States	10/06/1996	Granted	08/987084	US6339080
WO	10/06/1996	Gone National	PCT/GB96/01382	WO1996/041627

1.9 Schedule for Family P009 - Process

a. PCT Abstract
The invention provides a method of forming an iron hydroxypyrone compound comprising reacting a hydroxypyrone with a non-carboxylate iron salt in an aqueous solution, and precipitating the iron hydroxypyrone compound from the aqueous solution having a pH of greater than 7.

b. Ownership
This patent family is in the name of Iron Therapeutics Holdings AG.

c. Inventors
Michael Arthur Stockham

d. Summary of Invention and Commercial Context
PCT/GB2012/050160 was filed on 26 January 2012 claiming priority from GB1101370.3 filed on 27 January 2011, and published as WO2012/101442 on 2 August 2012. The application entered the national phases in Europe, US, Canada, Japan, Korea, China, Australia, Brazil, Hong Kong, India, Russia, Singapore and South Africa in July 2013. Any granted patents in this family will expire in January 2032.

The invention relates to a new method of forming iron hydroxypyrone complexes by reacting a hydroxypyrone with a non-carboxylate iron salt in aqueous solution at a pH above 7.

The Group does not use this method, however it blocks others from using the method and a product claim is also included which protects pharmaceutical compositions of FERACCRU that also contain iron hydroxide. Hence this family indirectly covers alternative methods of production of FERACCRU that would result in the production of iron hydroxide.

e. Prosecution
Patents have been granted in the US and Australia, and applications are currently pending in all other territories.

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The main method claim as pending in Europe is as follows:

"A method of forming an iron hydroxypyrone compound comprising reacting a hydroxypyrone with a non-carboxylate iron salt in an aqueous solution and precipitating the iron hydroxypyrone compound from the aqueous solution having a pH of greater than 7".

Claim 10 (product claim) as pending in Europe:

"A pharmaceutical composition comprising an iron hydroxypyrone compound and an iron hydroxide".

f. Family P009- Patent Summary Table

Country	Filing date	Status	Application number	Publication number
Europe	26/01/2012	Pending	12708368.1	EP2668175
US	26/01/2012	Granted	13/981551	Patent No. US9096629
US Divisional	26/01/2012	Pending	14/750462	US2015-0320863
China	26/01/2012	Pending	CN201280006090.4	CN103443091
Australia	26/01/2012	Granted	2012210337	AU2012210337
Brazil	26/01/2012	Pending	BR1120130187620	-
Canada	26/01/2012	Pending	2824931	CA2824931
Hong Kong (CN)	11/06/2014	Pending	14105483.7	1192229
Hong Kong (EP)	19/02/2014	Pending	14101565.7	1188452
India	26/01/2012	Pending	1402/MUMNP/2013	-
Japan	26/01/2012	Pending	2013-550951	JP2014503579
Korea	26/01/2012	Pending	2013-7022561	KR20140022377
Russia	26/01/2012	Pending	2013139544	-
Singapore	26/01/2012	Pending	201305698-1	SG192153
South Africa	26/01/2012	Pending	2013/05221	-
WO	26/01/2012	Gone National	PCT/GB2012/050160	WO2012/101442

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2. PT20

2.1 Schedule for PT20 Family P001 - Ligand modified poly oxo-hydroxy metal ion materials, their uses and processes for their preparation

a. PCT Abstract

Ligand-modified poly oxo-hydroxy metal ion materials and their uses are disclosed, in particular for nutritional, medical, cosmetic or biologically related applications for example for the treatment of a deficiency related to a component of the material or for the removal of an endogenous substance capable of binding to the material. The present invention further relates to processes for preparing the materials and optimising their physicochemical properties and their medical uses.

b. Ownership

This patent family is exclusively licensed by PTL from the Medical Research Council in the fields of phosphate binding for the treatment of renal diseases and/or intravenous iron for the treatment of iron deficiency anaemias.

c. Inventors

Jonathan Joseph Powell; Sylvaine Francoise Aline Bruggraber; Nuno, Jorge Rodrigues Faria; Dora Isabel Amaral Pereira.

d. Summary of Invention and Commercial Context

PCT/GB2008/000408 was filed on 6 February 2008 claiming priority from GB0702270.0 and US 60/888,386 both filed on 6 February 2007. The application published on 14 August 2008 as WO2008/096130 and entered the national phase in Australia, Brazil, Canada, China, Europe, UK, India, Japan, South Korea, Mexico, Israel, South Africa, Singapore, United States, Hong Kong and Eurasia in August 2009. The opposition period in Europe will expire on 17 March 2016. Any granted patents in this family will expire in February 2028 except for US8058462 which will expire in August 2029.

The invention relates to ligand-modified poly oxo-hydroxy complexes, their production and use and covers a broad range of applications, hence the field limitation of the exclusive licence. The complexes are defined according to the formula $M_xL_y(OH)_n$ where M is one or more metal ions, L is one or more ligands, where ligand incorporation into the complex is through identifiable bonding. The complex is for use as an iron supplement or for the removal or inhibition of an endogenous substance in the subject capable of binding to the complex.

This patent family provides PTL with broad comprehensive protection on the PT20 process and corresponding protection on the compositions produced by that process. PTL has the right to prevent others from importing PT20 produced by the claimed process into a territory where the process claim is in force (such as the US and any validated EP territory). Method

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of treatment / medical use claims, broadly protect PTL's intended use of PT20, including hyperphosphatemia.

e. Prosecution

Prosecution is ongoing in Brazil, Canada and India.

f. PT20 Family P001- Patent Summary Table

Country	Filing Date	Status	Application Number	Publication number
Australia	06/02/2008	Granted	2008212653	AU2008212653
Brazil	06/02/2008	Pending	PI0807212-4	-
Canada	06/02/2008	Pending	2676146	CA2676146
China	06/02/2008	Granted	200880004288.2	CN101627047
Eurasia	06/02/2008	Granted	200970718	EA200970718
Europe (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR)	06/02/2008	Granted	08709331.6	EP2125847
UK	06/02/2008	Granted	0802214.7	GB2451713
Hong Kong	06/02/2008	Granted	10105191.4	-
Israel	06/02/2008	Granted	199901	-
India	06/02/2008	Pending	2713/KOLNP/2009	-
Japan	06/02/2008	Granted	2009-548736	JP2010520856
Mexico	06/02/2008	Granted	MX/A/2009/008281	MX2009008281
South Africa	06/02/2008	Granted	2009/05083	ZA200905083
South Korea	06/02/2008	Granted	10-2009-7016904	KR20090121281
Singapore	06/02/2008	Granted	200904884-4	-
United States	06/02/2008	Granted	12/026,861	Patent No. US8058462
WO	06/02/2008	Gone National	PCT/GB2008/000408	WO2008/096130

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2.2 Schedule for PT20 Family P002

a. PCT Abstract

Phosphate binding materials and compositions comprising them which are solid ligand-modified poly oxo-hydroxy metal ion materials are disclosed that are based on ferric iron oxo-hydroxides modified with carboxylic acid ligands, or ionised forms thereof. These materials are made and tested in the examples provided in the application to demonstrate that they can bind phosphate in in vitro and in in vivo studies.

b. Ownership

This patent family is exclusively licensed by PTL from the Medical Research Council

c. Inventors

Jonathan Joseph Powell; Nuno, Jorge Rodrigues Faria

d. Summary of Invention and Commercial Context

This application was filed on 5 August 2009 as international application PCT/GB2009/001931 claiming priority from GB0814326.5 and US 61/086,244 both filed on 5 August 2008. The application published on 11 February 2010 as WO10/015827 and entered the national phase in Australia, Brazil, Canada, China, Europe, UK, Hong Kong, India, Japan, South Korea, Mexico, Singapore, Israel, South Africa, United States and Eurasia in February 2011. If granted an approximate expiry date will be August 2029.

The invention relates to a ferric iron composition for a medical use in the treatment of hyperphosphatemia, wherein the ferric iron composition is represented by the formula $M_xL_y(OH)_n$ wherein M represents one or more metal ions that comprise Fe^{3+} ions.

This patent family claims a narrower medical use not specifically disclosed in the earlier PT20 Family P001. Grant of the US patent provides PTL with strong protection covering the intended use of PT20 and the right to prevent third parties from labelling such a product for the treatment of hyperphosphatemia.

e. Prosecution

Prosecution is ongoing in Brazil, Canada, Europe, Hong Kong, India and South Korea.

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f. PT20 Family P002- Patent Summary Table

Country	Filing Date	Status	Application Number	Publication number
Australia	05/08/2009	Granted	2009278906	AU2009278906
Brazil	05/08/2009	Pending	PI0917503-2	-
Canada	05/08/2009	Pending	2732226	CA2732226
China	05/08/2009	Granted	200980134870.5	Patent No. ZL200980134870.5
Eurasia	05/08/2009	Granted	201170116	EA201170116
Europe	05/08/2009	Pending	09784878.2	EP2320884
UK	05/08/2009	Granted	0913684.7	GB2462374
Hong Kong	05/08/2009	Pending	11107662.9	-
India	05/08/2009	Pending	545/KOLNP/2011	-
Israel	05/08/2009	Granted	210913	IL210913
Japan	05/08/2009	Granted	2011-521635	JP2011529954
Mexico	05/08/2009	Granted	MX/A/2011/001258	MX294631
Singapore	05/08/2009	Granted	201100555-0	-
South Africa	05/08/2009	Granted	2011/00821	Patent No. 2011/00821
South Korea	05/08/2009	Pending	10-2011-7004981	KR20110052680
United States	05/08/2009	Granted	12/536,014	Patent No. 7,943,664
WO	05/08/2009	Gone National	PCT/GB2009/001931	WO2010/015827

3. Other Metal Patent Families

3.1 Schedule for Family P002 - Use of metal complexes to treat gastrointestinal infections

a. US6552072 Abstract

Compositions and methods for treating gastrointestinal symptoms and gastrointestinal microbes are provided. In accordance with the method, a dietary metal and a dietary ligand are administered, wherein the dietary metal is zinc, copper, cobalt, manganese or iron and the dietary ligand is ascorbate, aspartate, citrate, histidine, malate, maltol, gluconate, glutamate, glutamine, succinate, tartrate, or a combination thereof.

b. Ownership

This patent family is in the name of Iron Therapeutics Holdings AG.

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c. Inventors

Richard Paul Hepworth Thompson; Jonathan Joseph Powell; Rosemary Helen Phillips; Sylvaine Francoise Aline Chevalier.

d. Summary of Invention and Commercial Context

PCT/GB97/02797 was filed on 10 October 1997 claiming priority from GB9621273.3 filed on 11 October 1996, and published as WO98/16218 on 23 April 1998. The application entered the national phase in October 2000 in Canada, Europe, United States, Malaysia, Taiwan and South Africa. US6552072 is a divisional of US6197763 (now lapsed) and will expire in October 2017.

The invention relates to complexes of dietary metal ions for the treatment of gastrointestinal microbes, e.g. *H. pylori.*

The granted US patent US6552072 has a main claim as follows:

"An orally administrable pharmaceutical composition comprising a dietary metal, a dietary ligand and a pharmaceutically acceptable carrier, excipient or diluent,
wherein the dietary metal is selected from the group consisting of copper, cobalt, and manganese, or a salt thereof, and the dietary ligand is maltol (3-hydroxy-2-methyl-4-pyrone)".

The granted claims of US6552072 do not cover the FERACCRU formulation since iron as a dietary metal is not included. The patent prevents third parties from developing formulations in the US comprising maltol where iron is replaced with copper, cobalt or manganese, and is not relevant in respect of FERACCRU, but could be used to treat, for example, gastrointestinal infections caused by H. pylori (a cause of stomach ulcers).

e. Prosecution

Prosecution completed in all territories.

f. Family P002 - Patent Summary Table

Country	Filing date	Status	Application number	Publication number
United States	10/10/1997	Granted	09/758761	US6552072
WO	10/10/1997	Gone National	PCT/GB97/02797	WO1998/016218

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3.2 Schedule for Family P003 - Use of cobalt compounds to treat gastrointestinal infections caused by *H.pylori*.

a. PCT Abstract

Cobalt salts have been found to be particularly effective against H. pylori and may therefore be used to treat gastrointestinal infection with these bacteria. The cobalt salts have the advantage of showing a good degree of selectivity for H. pylori over other Gram positive and Gram negative bacteria. Treatment with the cobalt salts may be carried out at the same time as conventional treatment with an antibiotic and/or a proton pump inhibitor

b. Ownership

This patent family is in the name of Iron Therapeutics Holdings AG.

c. Inventors

Sylvaine Francoise Aline Bruggraber; Jonathan Joseph Powell.

d. Summary of Invention and Commercial Context

PCT/GB2001/002277 was filed on 24 May 2001 claiming priority from GB0012487.5 filed on 24 May 2000 and published as WO2001/089534 on 29 November 2001. The application entered the national phase in the UK and US in November 2002. The GB patent will expire in May 2021 and the US patent will expire in October 2017.

The invention relates to the treatment of H. pylori gastrointestinal conditions by administration of a cobalt salt.

The granted main claim of GB2379388 is as follows:

“Use of a cobalt salt comprising a non-polymeric anion in the manufacture of a medicament for selectively treating and/or preventing a gastrointestinal infection caused by H.pylori”.

Independent claim 11 is directed to a composition:

“A pharmaceutical composition which comprises a cobalt salt comprising a non-polymeric anion and which is adapted for the delayed release of cobalt ions over a period within the range of from 1 to 10 hours”.

The claims are limited to the presence of cobalt, therefore this family is not relevant in respect of FERACCRU but could be useful in the treatment of gastrointestinal infections caused by H. pylori (a cause of stomach ulcers).

e. Prosecution

Prosecution completed

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f. Family P003 - Patent Summary Table

Country	Filing date	Status	Application number	Publication number
Great Britain	24/05/2001	Granted	0229868.5	GB2379388
United States	24/05/2001	Granted	10/296486	Patent No. US7811609
WO	24/05/2001	Gone National	PCT/GB01/02277	WO 2001/089534

FREEDOM TO OPERATE

Potential infringement of third party intellectual property rights

Stratagem has conducted freedom to operate (FTO) searches and analyses to identify any third party patents that are relevant to the use of FERACCRU and PT20.

Broad patent and literature searches have been conducted by Stratagem in respect of FERACCRU and PT20. No patent families that cover FERACCRU per se were found. Stratagem have concluded, with input from the Group, that none of the patent families identified appear to pose an infringement risk to the Group in relation to the commercialisation of FERACCRU and PT20.

THE GROUP'S TRADE MARK PROTECTION

The Group's overall strategy has been to file trade mark applications for the core marks for the Group in the UK and European Union.

The following trade mark applications and registrations exist in the name of Iron Therapeutics Holdings AG:

Trade Mark	Summary
SIDEROMAL	This mark is used for ferrous iron and hydroxypyrone (family P004) and is registered as a word mark in the UK (registered no. 2241570, filed 04.08.2000) for "pharmaceutical preparations and substances; veterinary preparations and substances; medicines" in class 5, and EU application (application no. 13779277, filed 27.02.2015) covering all goods in class 5.

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HEMAXOMAL	This mark is registered as a word mark in the UK (registered no. 2346245, filed 17.10.2003) for "pharmaceutical preparations and substances; veterinary preparations and substances; medicines" in class 5.
FERACCRU	This mark is used for ferric trimaltol and is registered in the UK (registered no. 3059741, filed 13.06.2014) for "pharmaceutical preparations and substances; veterinary preparations and substances; medicines" in class 5, and registered in the EU (registered no. 12995486, filed 13.06.2014) covering "pharmaceuticals" in class 5 and "research of pharmaceuticals; testing of pharmaceuticals" in class 42.

No trade mark applications or registrations appear to exist in the names of Shield Holdings* or Phosphate Therapeutics*.

CONCLUSION AND GENERAL INTELLECTUAL PROPERTY STATEMENTS

Stratagem is not aware of any challenges or disputes relating to any of the patents, patent applications, trade marks or trade mark applications discussed above.

Stratagem is not aware of any prospective or alleged infringement by third parties of any of the patents, patent applications, trade marks or trade mark applications owned or exclusively licensed to the Group.

Stratagem is not aware of any particular circumstances which might affect the patents, patent applications, trade marks or trade mark applications of the Group or the validity, enforceability, subsistence or registration of such rights.

Stratagem is not aware of any suspected or alleged infringement of third party intellectual property by the Group.

Yours Faithfully,

Nicola Baker-Munton, CPA, EPA

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APPENDIX I

GENERAL OVERVIEW OF PATENTS AND TRADE MARKS

Background to the Patent System

Below is a brief outline of the procedures and requirements whereby patents are filed in the United Kingdom and are then subsequently prosecuted to grant on an international basis.

The patent system exists to reward and promote innovation. A monopoly right is granted to the patent owner for a fixed period of time. In return the patent owner publishes an enabling disclosure of the invention. An invention must meet several criteria if it is to be eligible for patent protection. These include, most significantly, that the invention must consist of patentable subject matter, the invention must be industrially applicable (useful), it must be new (novel), it must exhibit a sufficient "inventive step" (be non-obvious), and the disclosure of the invention in the patent application must meet certain standards.

A patent is territorial. For example, a US patent gives the owner rights only in the US. It is generally advisable to seek patent protection in commercially important territories where any product of the invention is to be made or sold, or where any process or method of the invention is to be used.

There is no such thing as a single international or world-wide patent. In order to obtain patent protection for an invention overseas, it is necessary, in most cases, to file separate national patent applications in each country in which protection is sought, and to prosecute each patent application before the corresponding national patent office. However, the PCT system may be used for filing international patent applications, which helps to streamline at least the early stages of the international patenting procedure, and effectively postpones the need to file national patent applications.

The international patent system is established by the PCT and administered by the WIPO. An international application can be made under the PCT, and applicants may designate over 140 states, either separately or by way of regional designations such as a European patent application. The PCT application is ultimately converted into a number of national and/or regional patent applications, which are then examined again to meet national/regional requirements for the purposes of grant.

Patents are frequently referred to as "monopolies", but a patent does not give the right to the inventor or the owner of a patented invention to make, use or sell anything. The effects of the grant of a patent are that the patented invention may not be exploited in the country by persons other than the owner of the patent unless the owner agrees to such exploitation. Thus, while the owner is not given a statutory right to practise his invention, he is given a statutory right to prevent others from commercially exploiting his invention, which is frequently

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referred to as a right to exclude others from making, using or selling the invention. The right to take action against any person exploiting the patented invention in the country without his agreement constitutes the patent owner's most important right, since it permits him to derive the material benefits to which he is entitled as a reward for his intellectual effort and work, and compensation for the expenses which his research and experimentation leading to the invention have entailed.

It should be emphasised, however, that while national governments may grant patent rights, they will not enforce them. It is up to the patent owner or exclusive licensee to bring an action, usually under civil law, for any infringement of his patent rights. The patentee must, therefore, be his own "policeman."

A patent is a negative right to exclude others, not a positive right to practise an invention. Owning a patent or having a licence to a patent gives no automatic right to practise the invention covered by the patent, since using the patented invention may infringe a patent held by a third party. It is therefore important to establish whether a patent owner has the "freedom to operate" his invention without risk of infringing patents that are held by others (which we consider in respect of the Group above).

Freedom to operate searches are reliant on the efficacy and veracity of the information provided by the respective Patent Offices to the database suppliers. Patent publications are often given an enhanced title and abstract based on the database supplier's interpretation of the publication and the search is based upon these enhanced terms. Errors or omissions in the databases can reduce the accuracy of a search so there can never be absolute certainty that freedom to operate search results capture all relevant patents.

Obtaining patent protection

To obtain grant of a patent in one or more territories the typical procedure for a UK resident is described in more detail below. The first application to be filed, which is called the 'priority' or 'basic' application, will be at a national patent office, in the case of a UK resident, usually at the UKIPO. Within twelve months of the priority application, a decision must be made as to whether protection is required elsewhere in the world. These patent applications may be international, regional and/or foreign national applications claiming priority from the priority application, i.e. benefiting from the earlier date of that filing. In the typical example, a single PCT application designating all states should suffice.

Whilst the patent application is in the international phase (i.e. is still a PCT filing), a literature search will be carried out by a designated Patent Office on behalf of WIPO (the organisation which administers the PCT), to determine the extent of the prior art and produce a preliminary non-binding opinion on the patentability of the invention (the Written Opinion). Still in the international phase, publication of the application will occur eighteen months from the earliest priority date. This publication may be the first opportunity for

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interested third parties (including competitors) to study the invention and the scope of the claims.

The National Patent offices in most countries (or in the case of a European application the Regional office, which is the EPO) then carry out substantive examination. This may refer to the International Preliminary Examination but often raises further objections. The examination aims to determine the scope of protection to which an applicant is entitled, having regard to the prior art, and the extent to which the applicant has effectively described the invention, in accordance with National/Regional, as opposed to International laws. In most cases, applications are filed with relatively broad claims which are narrowed by way of amendment in the course of substantive examination.

Following what may be several years of prosecution in each country, by now following its own timetable and acting independently of the others, the application(s) will hopefully be granted. It is at this point that the patent owner actually receives his/her 'monopoly' and right to stop others through enforcement of the patent in the territory. Part of the grant procedure is publication of the patent in its granted form i.e. including any amendments made during prosecution. When a European patent application is granted, it must be validated (turned into a national patent) in each of the European states of interest. There are currently over 30 European countries that are part of the European system (EPC). Following the grant of the patent by the EPO, the patent owner must select in which of the European countries to obtain a granted patent. The costs at this stage can be significant, due mainly to the costs of any translation, thus it is usual to limit European validation to the most important European markets.

European patents may be opposed within a nine month opposition period which runs from the date of grant. This opposition term provides a mechanism by which all patents arising from the European application can be challenged together before the EPO. Granted patents in any territory may be challenged for validity by a third party before the National courts at any time throughout the life of the patent. However, in general a granted patent carries a presumption of validity, and good evidence and/or arguments must be presented to revoke the patent or to force a limitation of the scope of the claims.

Ownership of a Patent

According to UK law, the right to apply for and be granted a patent primarily accrues to the inventor or inventors, but by act of law or agreement that right may belong to another. This provision includes employee inventors whose inventions are generally considered to belong to the employer, in particular where their duties are such that they can reasonably be expected to invent, or where they are in such a position within the company (such as a managerial position), that they can be expected to further the interests of their employer by the making of an invention.

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Patent Term
In general, a patent is granted for the term of up to twenty years from filing. By virtue of the Paris Convention, a year prior to this called the 'priority' or 'convention' year will be recognised for the purpose of establishing the date of first filing in most territories. This first year is not used in the calculation of the twenty-year term.

Data Exclusivity
The data exclusivity provisions in Europe are an automatic right and provide for a maximum period of 10 years from the first marketing authorisation before a competitor can place that product on the market using the clinical trial data (Directive 2004/27/EC). A 1 year extension for a new use may also be available. A competitor may apply for a marketing authorisation after 8 years. This runs in parallel to the patent term and once the patent has expired a competitor is free to conduct their own clinical trials.

The data exclusivity provisions in the US are similar, typically allowing for a period of 5 years data exclusivity following US Food and Drug Administration (FDA) approval provided that the product has not previously been approved. The Group will be using the 505(b)(2) approval route and so will be entitled to 3 years data exclusivity. The 505(b)(2) route allows the FDA to rely on data not developed by the applicant for a new drug application (NDA).

Regulatory Approval in the US and Orange Book Listing.
The FDA's publication "Approved Drug Products with Therapeutic Equivalence Evaluations", also known as the Orange Book, identifies drug products approved on the basis of safety and effectiveness by the FDA under the Federal Food, Drug and Cosmetic Act.

Innovator companies have the opportunity to list composition and method of use patents that cover the drug compound and this has the advantage that generic companies intending to make or sell a drug that arguably infringes the listed patent must by law notify the patent owner of possible infringement (also known as a paragraph IV certification). Once notified the patent owner can file a lawsuit for patent infringement within 45 days of notification and provided they do this a 30 month stay is triggered before the generic company can sell the drug, subject to FDA approval.

Currently the Orange Book only lists "composition" or "method of use" patents, for example particular formulations, polymorphs, dosages and methods of treating certain diseases. Process patents covering methods of manufacture are not permitted to be listed.

Renewal Fees
Renewal fees to maintain a granted patent and/or a pending application (in the case of a European patent application) are usually payable annually. In the United States renewal fees are paid 3.5, 7.5 and 11.5 years from the date of patent grant. Failure to pay renewal fees

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results in an automatic loss of patent rights. It is, therefore, important that an appropriate system is in place to ensure that renewal fees are paid.

Obtaining Trade Mark Protection

To obtain registration of a trade mark in one or more territories the typical procedure for a UK resident would be to conduct an identical screening search to see if the mark is already registered in the core countries of the UK, EU and US and then file a first application which is called the 'priority' or 'basic' application at either the UK IPO or OHIM (the Community TMO). The application will then be examined by the selected office on the basis of absolute grounds for registration, i.e. if the mark is considered to not be distinctive, or to be descriptive of a characteristic of the goods/services, or to be offensive in some way such as being immoral or incorporating protected emblems, it will be refused. Although the selected office will conduct a limited search for earlier conflicting marks, it will not refuse the application on this basis. The selected office will also review the specifications (descriptions) of goods and services filed with the application and raise any concerns. Normally a two month period is allowed to respond to any objections. Once the application is accepted, it will be published and up to 3 months are allowed for third parties to file formal opposition. If no oppositions are filed, the Registration Certificate will issue.

Within six months of the priority application, it is recommended that foreign applications are filed to protect the mark in other countries. Such foreign trade mark applications may be international, regional and/or foreign national applications claiming priority from the priority application, i.e. benefiting from the earlier date of that filing. It is not mandatory to file by this date and applications may be filed later, but they will then not benefit from the earlier priority filing date. A typical example would be either a national filing in the US, or an International Application covering the US, Japan, China and various other states which are members to the Madrid Protocol.

If an International Application is filed, WIPO will examine the application again on absolute grounds and raise any objections, but if the application is acceptable, an International Registration Certificate will issue and the registration is published and details sent to each of the countries designated in the original application. A period of 12 or 18 months is then allowed for each country to examine the International Registration under its local laws and publish the mark once the International Registration is accepted. If nothing is heard from the national office within the 12 or 18 month period set, the International Registration is assumed to have force in the relevant country.

National Applications are examined by their local Trade Mark Office and objections may be raised on the basis of absolute grounds (explained above) or relative grounds (i.e. earlier conflicting marks). Once any such objections have been overcome the application will be accepted and published. If no oppositions are filed within the time limit set by the national office, the application will be registered and the Registration Certificate will issue. In some countries such as the US and Canada, it is normally necessary to prove use before a mark can

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be registered, but there are also ways of by-passing this requirement by basing the foreign application on home registrations.

On average it takes 4-8 months to achieve registration in the UK, 9-12 months in the EU and 18-24 months in the US and Canada. Once the mark is registered, the proprietor actually receives the 'monopoly' right to stop others using conflicting marks through enforcement of the trade mark in the pertinent territory.

Registered trade marks in any territory may be challenged for validity by a third party before the national TM offices or courts at any time throughout the life of the trade mark on the basis of non-use, earlier rights or that the registered mark has become generic or misleading. However, in general a registered trade mark carries a presumption of validity, and good evidence and/or arguments must be presented to revoke the trade mark or to force a limitation of the scope of the registration.

Ownership of a Trade Mark
According to UK law, the right to apply for and be granted a trade mark primarily accrues to the person or company which first uses the mark. Care needs to be taken in relation to logos or stylised marks which may also have copyright. Copyright will remain with the original creator until it is assigned in writing, signed by the assignee, to the commissioner. If the person who created the logo is an employee, the copyright will belong to the employer as long as the work in creating the logo was a reasonable part of their employed role. It is advisable to obtain an executed assignment even from employees to avoid argument later.

Trade Mark Term
In general, a trade mark is initially registered for a standardised term of 10 years from filing, but this may vary from country to country and can be between 7 and 14 years. Also the term may run from the date of registration, or a priority date, rather than the date of filing.

Renewal Fees
Renewal fees are payable at the end of each 10 year term (or whatever is the term dictated by local law). Trade Mark registrations may be renewed indefinitely meaning that if the mark is in use and therefore not at risk of cancellation, it may be registered for decades – longer than any other intellectual property right. Failure to pay renewal fees results in an automatic loss of trade mark rights. It is, therefore, important that an appropriate system is in place to ensure that renewal fees are paid on time, particularly in view of the long gap between payments which means that they are easy to forget.

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PART 8

MARKET REPORT

REPORT

Prepared for Shield Therapeutics PLC & Liberum Capital Limited ("Liberum")

12 February 2016

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INTRODUCTION

The Directors

Shield Therapeutics PLC

Northern Design Centre

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Liberum Capital Limited

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London

EC2Y 9LY

12 February 2016

Dear Sirs,

GfK UK Limited (“GfK”), is part of the GfK Group, which was established in 1934. GfK’s market access team is a leading consultancy specialising in the assessment of healthcare companies, projects, products and markets and assisting in their development. Over the past 20 years GfK has prepared public and private placing documents for development stage biotechnology, pharmaceutical, medical devices and life sciences companies. In addition, many due diligence assignments have been successfully completed on behalf of international investors. GfK employs specialists with knowledge of science, technology, product development, markets and business issues in medicine and life sciences.

GfK has been instructed by Shield Therapeutics PLC ("Shield Therapeutics" or "Shield") to assess and review certain aspects of Shield Therapeutics’ business namely:

- How well the company’s key products are viewed in the marketplace
- The potential market for the key products
- What price is likely to be acceptable for the products

GfK has focused its investigations on Germany, Spain, the UK, and the US markets and has focused the majority (80%) of research time on Feraccru, and the remaining time on PT20.

In preparing this report GfK’s consultants have: Conducted interviews with some of the key Company staff and officers, reviewed the documentation provided by Shield Therapeutics and assessed its activities with reference to the proprietary knowledge base possessed by GfK. In addition, the documentation supplied by Shield Therapeutics has been supplemented by GfK’s own interviews with external independent experts.

For the purpose of Prospectus Rule 5.5.3R(2)(f), we are responsible for this report as part of the Prospectus and declare that we have taken all reasonable care to ensure that the information contained in this report is, to be best of our knowledge, in accordance with the facts and contains no omission likely to affect its import. This declaration is included in the Prospectus in compliance with item 1.2 of Annex 1 to the PD regulation.

METHODOLOGY AND OBJECTIVES

GfK conducted a limited programme of desk research to review each of the company's areas of operation, supplemented by the feedback from a face to face meeting with the company. Shield Therapeutics has conducted external independent reports on which GfK's research is based, supplemented with limited additional research.

A workshop was held with GfK internal experts, to conduct a rigorous in-house assessment and critique of Shield Therapeutics' value proposition to potential investors. The output from this was a 'gap analysis' which was fed into the scope of the primary research phase.

Primary market research was conducted to validate the market opportunity for Feraccru (Inflammatory Bowel Disease (IBD) and Chronic Kidney Disease (CKD) and PT20 (Hyperphosphataemia). The programme of primary market research included in-depth interviews with Key Opinion Leaders (KOLs), gastroenterologists, nephrologists and payers in order to validate the research that had already been carried out, as well as fill in any gaps in the data and ensure that GfK is satisfied with the expert report product opportunity claims.

The number of interviews carried out in the selected markets is outlined in Table 1.

Table 1: Number of IDIs carried out in each market

Markets	KOL/Clinicians	Payers
US	10	5
UK	6	3
Germany	6	3
Spain	6	3
Total	**28**	**14**

In addition to the in-depth telephone interviews, GfK also carried out a 10 to 15 minutes online questionnaire survey with prescribers across the US, the UK, Germany and Spain. The focus of the survey was Feraccru, as this product is closest to market and assumed to be of greatest investor interest. Both gastroenterologists and nephrologists were surveyed, to gain opinion on Feraccru's potential in iron deficiency anaemia (IDA) in inflammatory bowel disease and chronic kidney disease. The number of physicians recruited is included in Table 2.

Table 2: Number of online survey physicians recruited

Markets	Gastroenterologists	Nephrologists
US	90	40
UK	30	20
Germany	30	20
Spain	30	20
Total	**180**	**100**

FINDINGS

Management group capabilities

Shield Therapeutics has a strong, experienced senior team, with extensive development and commercialization experience. The team has recently been strengthened with the hiring of Paul Steckler, Vice President-Commercial Operations,Dr Mark Sampson (VP, Regulatory Affairs), Kate Hopkinson (Marketing Director) and Emma Chaffin (UK Managing Director). The company has retained the use of a recruitment consultant to find talented people to fill the gaps within the team.**Feraccru**

Epidemiology

Number of patients

Iron deficiency anaemia (IDA) is a severe stage of iron deficiency in which haemoglobin (or the haematocrit) declines below the lower limit of normal. IDA is defined as anaemia with biochemical evidence of iron deficiency. IDA occurs when iron stores are exhausted and the supply of iron to the bone marrow is compromised.

WHO defines IDA as a Haemaglobin of less than 13 g/dl for males and less than 12 g/dl for females in normal populations. This definition is used widely in guidelines including ECCO (IBD) and KDOQI (CKD) in both Europe and the US.

IBD

Anaemia is a common complication of inflammatory bowel diseases (IBD), with multiple causes, although iron deficiency is the most prevalent. Almost every anaemic patient with IBD demonstrates some degree of iron deficiency as a consequence of dietary restrictions, malabsorption, or intestinal bleeding. Many other causes of anaemia exist in IBD, but are generally less common.[1]

Multiple studies have shown that, in a variety of populations with IBD the prevalence of IDA ranges from 14% to 76%.[2] [3] According to a 2014 Europe-wide systematic review and individual patient data

[1] Gasche C, Berstad A, Befrits R, Beglinger C, Dignass A, Erichsen K, Gomollon F, Hjortswang H, Koutroubakis I, Kulnigg S, Oldenburg B, Rampton D, Schroeder O, Stein J, Travis S, Van Assche G. Guidelines on the diagnosis and management of iron deficiency and anemia in inflammatory bowel diseases. Inflamm Bowel Dis. 2007 Dec;13(12):1545-53.
[2] Filmann N, Rey J, Schneeweiss S, Ardizzone S, Bager P, Bergamaschi G, Koutroubakis I, Lindgren S, Morena Fde L, Moum B, Vavricka SR, Schröder O, Herrmann E, Blumenstein I. Prevalence of anemia in inflammatory bowel diseases in

meta-analysis on 2192 patients, who were mainly treated in tertiary referral centres, the overall prevalence of anaemia in IBD patients was 24% (95% confidence interval, 18-31).[4] 57% of the anaemic patients were iron deficient (i.e. an overall prevalence of IDA in IBD of 14%). In other studies, IDA prevalence in IBD patients ranges from 36% to 76%.[5] In the estimates of potential patient populations, GfK has used a prevalence of 40%, taking an estimate based on the size and age of the studies which evaluated IDA prevalence.

CKD

In patients with Chronic Kidney Disease (CKD), as kidney function declines and in patients with more advanced CKD stages, the incidence and prevalence of anaemia increases.[6] A UK observational study was carried out (N=1,099,292) with a nationally representative sample using anonymised routine primary care data from 127 Quality Improvement in CKD trial practices.[7] In this study, 25.3% of people with CKD had World Health Organization defined anaemia; 8.6% had Hb ≤ 11 g/dl; 3% Hb ≤ 10 g/dl; and 1% Hb ≤ 9 g/dl. Table 3 shows how the prevalence of anaemia in patients with CKD increases as the CKD becomes more advanced.

European countries: a systematic review and individual patient data meta-analysis. Inflamm Bowel Dis. 2014 May;20(5):936-45.

[3] Stein J, Hartmann F, Dignass AU. Diagnosis and management of iron deficiency anemia in patients with IBD. Nat Rev Gastroenterol Hepatol. 2010;7(11):599–610

[4] Filmann N, Rey J, Schneeweiss S, Ardizzone S, Bager P, Bergamaschi G, Koutroubakis I, Lindgren S, Morena Fde L, Moum B, Vavricka SR, Schröder O, Herrmann E, Blumenstein I. Prevalence of anemia in inflammatory bowel diseases in European countries: a systematic review and individual patient data meta-analysis. Inflamm Bowel Dis. 2014 May;20(5):936-45.

[5] Stein J, Hartmann F, Dignass AU. Diagnosis and management of iron deficiency anemia in patients with IBD. Nat Rev Gastroenterol Hepatol. 2010;7(11):599–610

[6] Kidney Disease: Improving Global Outcomes (KDIGO) Anemia Work Group. KDIGO Clinical Practice Guideline for Anemia in Chronic Kidney Disease. Kidney inter., Suppl. 2012; 2: 279–335.

[7] Dmitrieva O, de Lusignan S, Macdougall IC, Gallagher H, Tomson C, Harris K, Desombre T, Goldsmith D. Association of anaemia in primary care patients with chronic kidney disease: cross sectional study of quality improvement in chronic kidney disease (QICKD) trial data. BMC Nephrol. 2013 Jan 25;14:24. doi: 10.1186/1471-2369-14-24.

Table 3: Prevalence of anaemia in patients with CKD[8]

Class CKD		Hb < 13 g/dl (M)* Hb < 12 g/dl (F)		Hb > 11 g/dl		Hb ≤ 11g/dl**		Hb ≤ 10g/dl***		Hb ≤ 9 g/dl	
		N	%	N	%	N	%	N	%	N	%
eGFR > 90	F	11545	18.5%	61287	92.8%	4732	7.2%	1523	2.3%	536	0.8%
	M	3552	6.3%	54902	98.6%	790	1.4%	340	0.6%	142	0.3%
eGFR 60-89	F	16032	11.1%	132285	96.0%	5455	4.0%	1747	1.3%	612	0.4%
	M	7228	6.0%	106310	98.8%	1281	1.2%	541	0.5%	235	0.2%
Stage 3A	F	4542	14.3%	28205	94.5%	1654	5.5%	508	1.7%	173	0.6%
	M	2997	20.4%	12760	95.1%	657	4.9%	254	1.9%	101	0.8%
Stage 3B	F	2340	36.4%	5065	82.6%	1065	17.4%	329	5.4%	96	1.6%
	M	1616	48.7%	2654	83.5%	523	16.5%	207	6.5%	86	2.7%
Stage 4	F	663	59.8%	680	63.6%	389	36.4%	167	15.6%	35	3.3%
	M	553	71.3%	516	69.2%	230	30.8%	102	13.7%	38	5.1%
Stage 5	F	128	61.2%	108	55.1%	88	44.9%	43	21.9%	16	8.2%
	M	176	81.5%	123	59.4%	84	40.6%	38	18.4%	18	8.7%
CKD stage 3-5	F	7673	19.4%	34058	91.4%	3196	8.6%	1047	2.8%	320	0.9%
	M	5342	28.1%	16053	91.5%	1494	8.5%	601	3.4%	243	1.4%
Total CKD 3-5		13015	25.3%	50111	91.4%	4690	8.6%	1648	3.0%	563	1.0%

* WHO anaemia definition for adult males. ** NICE – UK guidelines. *** FDA recommended level for anaemia correction

Number of patients undergoing treatment

IBD

In the United States, it is currently estimated that about 1 to 1.3 million people suffer from IBD,[9] where the prevalence of ulcerative colitis is 249 per 100,000 persons and 319 per 100,000 persons

for Crohn's disease.[10] There is a lack of understanding of how many people experience IBD because there are no standard criteria for diagnosing, and identifying cases of IBD is often inconsistent or the disease may be classified as another condition.

In Europe, the prevalence rates for ulcerative colitis are 505 per 100,000 persons and for Crohn's disease are 322 per 100,000 persons,[11] with an estimated 2.5 million people suffering from IBD.[12]

Using data collected by GfK in an online survey, with gastroenterologists in the US (n=90), Germany, Spain and UK (n=90), estimates can also be made as to the percentage of IBD patients that are being pharmacologically treated for IDA. These results are shown in Table 4.

In the US, of the IBD patients seen by gastroenterologists who participated in the online survey, an average of 44% [range 0 to 100%] were treated with oral ferrous products (OFPs), 14% [range 0 to 65%] with IV iron and 42% [range 0 to 95%] received no iron supplementation. In Europe these figures were 31% [range 0 to 100%] treated with OFPs, 22% [range 0 to 90%] receiving IV iron and 45% [range 0 to 90%] receiving no iron supplementation.

As can be seen from the range of responses, there were wide variations in practice, which may reflect the severity of the patients seen by respondents, as well as variations in prescribing practice and individual preferences for oral vs. IV iron.

Table 4: Estimates of IBD population (patients/percentage) who are treated for IDA

Parameter	IBD
United States	
Prevalent population with IBD	1 million to 1.3 million
% with IDA	40% (400,000 to 520,000)
% receiving oral iron therapy	44% (176,000 to 228,800)
% receiving IV iron therapy	14% (56,000 to 72,800)
% receiving no iron supplementation	42% (168,000 to 218,400)
Europe	
Prevalent population with IBD	2.5 million
% with IDA	40% (1 million)
% receiving oral iron therapy	31% (310,000)
% receiving IV iron therapy	24% (240,000)
% receiving no iron supplementation	45% (450,000)

GfK assumes similar rates of IDA in IBD in the US and Europe

Based on these estimates, it would suggest that in the US there between 400,000 and 520,000 patients with IBD who have the potential to be being treated for IDA, and in Europe this figure is

[9] Centers for Disease Control and Prevention. Epidemiology of the IBD. http://www.cdc.gov/ibd/ibd-epidemiology.htm Accessed July 2015
[10] Molodecky, N.A. et a. Increasing incidence and prevalence of the inflammatory bowel diseases with time, based on systematic review. Gasteroenterology, 2012. 142:46-54.
[11] Molodecky, N.A. et a. Increasing incidence and prevalence of the inflammatory bowel diseases with time, based on systematic review. Gasteroenterology, 2012. 142:46-54.
[12] IBDBiom. Inflammatory Bowel Disease Biomarkers Programme. http://www.ibdbiom.eu/community/ Accessed 19 July 2015

approximately 1 million. These figures are broadly in-line with those projected by Shield Therapeutics' own commercial expectations.

These figures assume that all the prevalent population with IBD are being managed by gastroenterologists. In reality, this would not be the case. IBD is a condition which is characterised by active and inactive periods, and patients are likely to only need treatment when their condition is active. In addition, much of the data is from patients being treated in tertiary centres (i.e. the data on which patients are being pharmacologically treated, and the data on patients who have IDA). Patients who are managed by their GP will most likely not be captured in these above estimates.

From the primary research conducted, Shield's assumed peak penetration rate in IBD appears to be conservative. This rate is reasonable, particularly if Shield Therapeutics are able to show non-inferiority vs. IV iron.

CKD

Data on CKD are scarce, coming from medical databases and population surveys, with CKD data from medical databases tending to overestimate the prevalence of diseases.[13] The stages of CKD are mainly based on measured or estimated GFR (Glomerular Filtration Rate). There are five stages but kidney function is normal in Stage 1, and minimally reduced in Stage 2, as described in Table 5.

Table 5: KDOQI stages of kidney disease

Stage	GFR*	Description	Treatment
1	90+	Normal kidney function but urine findings or structural abnormalities or genetic trait point to kidney disease	Observation, control of blood pressure
2	60-89	Mildly reduced kidney function, and other findings (as for stage 1) point to kidney disease	Observation, control of blood pressure and risk factors
3A 3B	45-59 30-44	Moderately reduced kidney function	Observation, control of blood pressure and risk factors
4	15-29	Severely reduced kidney function	Planning for endstage renal failure
5	<15 or on dialysis	Very severe, or endstage kidney failure (sometimes called established renal failure)	Treatment choices

* All GFR values are normailsed to an average surface area of 1.73m^2

Data on the prevalence of CKD Stages 3, 4 and 5 from population surveys are summarised in Table 6.

[13] Zoccali C, Kramer A, Jager KJ. Chronic kidney disease and end-stage renal disease. NDT Plus (2010_ 3: 213-224

Table 6: Studies estimating the prevalence of CKD stages 3 -5

Study details	N	CKD stage 3	CKD stage 4	CKD stage 5
Health Survey for England[14]	>6,000	6% (males); 7% (females)		
NEOERICA study in the UK[15]	38,262	Overall prevalence of CKD stage 3-5 of 8.5%		
National Health and Nutrition Examination Survey, US[16]	12,785	5.4%	0.4%	

The prevalence of stage 3–5 CKD in population-based studies ranges from 3.57% (Norway) to 7.2% (Germany) in males and from 6.2% (Italy) to 10.2% (Iceland) in females. The prevalence of stage 3–5 CKD appears reasonably similar across EU countries,[17] and in these calculations, GfK has assumed a prevalence of 6% for CKD Stage 3 and 0.5% for CKD Stage 4, for the adult population in Europe. For the US, GfK has assumed a higher prevalance rate of 8% for CKD stage 3, based on more up to date prevalence study data.[18]

Based on estimates of patient numbers from dialysis registries, and published sources, the number of CKD patients with stage 3, stage 4 and stage 5 disease can be estimated across the US and EU markets. Using data collected by GfK in an online survey, with nephrologists in the US (n=40), and in Germany, Spain and UK (n=60), estimates can also be made as to the percentage of each group that are being pharmacologically treated. These results are shown in Table 7.

Findings from the online survey demonstrate that as patients progress from CKD stage 3 and develop more severe disease the use of OFPs decreases, as the use of IV iron increases, as does the overall percentage of patients who need treatment for IDA.

[14] Roth M, Roderick P, Mindell J (2011) Kidney disease and renal function. In: Craig R, Mindell J, editors. Health survey for England, 2010 (Vol. 1). Leeds: The NHS Information Centre for health and social care.
[15] Stevens PE, O'Donoghue DJ et al. (2007) Chronic Kidney disease management in the United Kingdom: NEOERICA project results. Kidney International (2007) 72: 92–9.
[16] Prevalence of Chronic Kidney Disease and Associated Risk Factors – Unite States, 1999-2004. MMWR March 2, 2007/56(08);161-165
[17] Zoccali C, Kramer A, Jager KJ. Chronic kidney disease and end-stage renal disease. NDT Plus (2010_ 3: 213-224
[18] Coresh J, Selvin E, Stevens LA, Manzi J, Kusek JW, Eggers P, Van Lente F, Levey AS. Prevalence of chronic kidney disease in the United States. JAMA. 2007 Nov 7;298(17):2038-47.

Table 7: Estimates of CKD patients who are treated for IDA

Parameter	CKD Stage 3	CKD Stage 4 (non-dialysis)	CKD Stage 5 (dialysis)
United States			
Potential number of patients	20.3 million*	1,268,000*	471,100[19]
% with IDA**	4% (812,000)	15% (192,000)	20% (94,200)
% receiving oral iron therapy	30% (243,600)	5 (67,200)	14% (13,188)
% receiving IV iron therapy	10% (81,200)	19% (36,480)	63% (59,350)
% receiving no iron supplementation	60% (487,200)	46% (88,320)	23% (21,700)
Europe (EU5)			
Number of patients	16.1 million	1,342,600	216,950[20]
% with IDA**	11% (1.771m)	34% (456,500)	43% (93,300)
% receiving oral iron therapy	30% (531,300)	36% (164,300)	7% (6,500)
% receiving IV iron therapy	10% (177,100)	21% (95,900)	77% (72,000)
% receiving no iron supplementation	60% (1.062m)	43% (196,300)	16% (15,000)

Percentages may not add up due to rounding

* Based on adult population (age > 15yrs) estimates taken from Eurostat for EU5 and United States Census Bureau, and a prevalence of 8% for CKD stage 3 amd 0.5% for CKD stage 4 in the US

** Based on mean estimates from Dmitrieva O, et al. BMC Nephrol. 2013 Jan 25;14:24, using FDA cut-offs for US calculations, and NICE cutoffs for European calculations.

Based on estimates of the number of CKD patients with IDA, GfK believes that Shield is taking a conservative view on the prevalence of IDA in CKD, with a combined target patient population in the US and Europe of 1.8 million (Shield) compared to 3.4 million (GfK).

Based on currently available information, Shield's penetration rates appear to be conservative. CKD patients are assumed to have a higher level of tolerance to OFPs than IBD patients, thus the penetration rate is likely to be lower in this group of patients than IBD patients.

These figures do not take into account the number of patients with IDA and CKD who are actually currently diagnosed and treated based on our sample, so there is a risk that the target numbers are too high. However, given the conservative prevalence used by Shield, this risk is somewhat mitigated.

[19] Based on estimates from Decision Resources 2014, with data sourced from US and EU renal registries
[20] Based on estimates from Decision Resources 2014, with data sourced from US and EU renal registries

Estimates of patients who are currently treated with IV iron products give a benchmark for the initial target population for Feraccru (i.e. switch patients). Estimates of CKD patients currently taking IV iron are 162,000 in the US and 322,000 in Europe.

Current unmet needs

Due to the limitations associated with the use of currently available oral ferrous products (OFPs), there are a number of clinical unmet needs associated with the use of these treatments:

- A reduction in adverse events related to the gastrointestinal tract
- An improvement in adherence to therapy
- An improvement in duodenal absorption due to concomitant gastrointestinal pathologies (IBD or any other cause of chronic inflammation, malignancy)
- A reduction in the length of the course of treatment needed to resolve anaemia (1-2 months) and replenish body iron stores (another 3-6 months, with the realisation that if the underlying cause of IDA is not addressed, the IDA may return and will require another course of treatment)

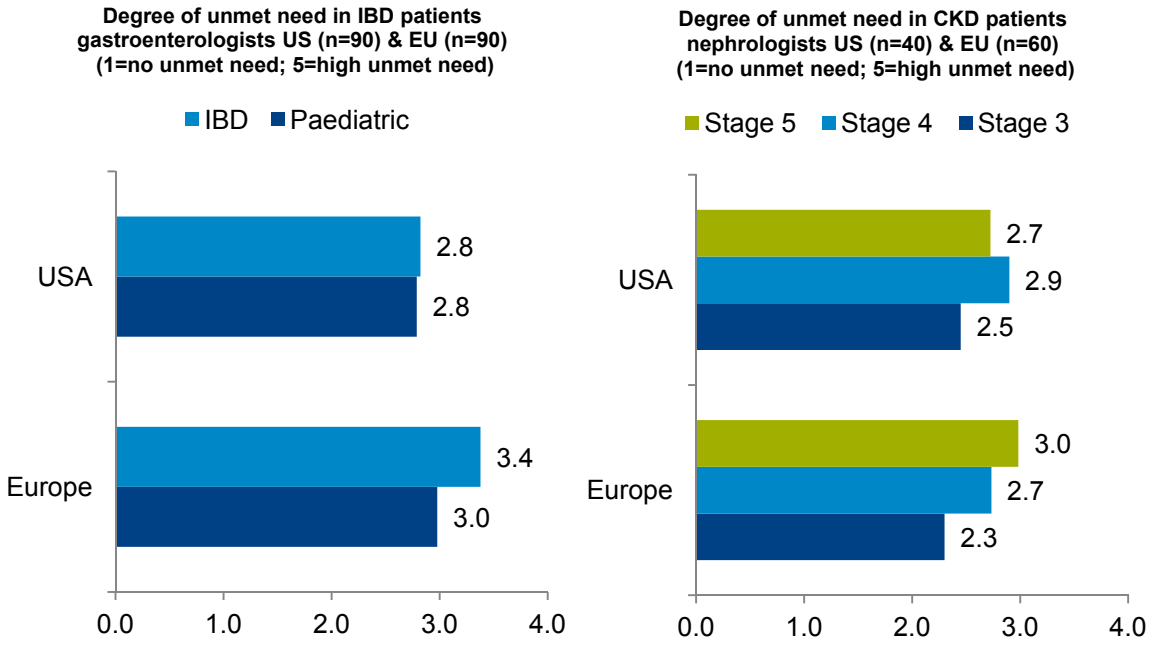
Non-adherence with current OFPs is common and, even in adherent patients, poor intestinal absorption fails to compensate for the iron need in the presence of ongoing blood losses or in inflammatory conditions with currently available OFPs.

Whilst the use of IV iron can address some of these unmet needs, these products are not without their own unmet needs:

- Risk of hypersensitivity/anaphylactic shock (particularly with the older IV iron products)
- Inconvenience and cost associated with visiting the hospital to receive treatment

In the online survey, respondents were asked to score, on a scale of 1 to 5 what level of unmet need they thought there is with regards to treatments for IDA associated with CKD (nephrologists) and IDA associated with IBD (gastroenterologists), and the results of this are shown in Figure 1.

Figure 1: Degree of unmet need for treatment for IDA in IBD and IDA in CKD (US&EU)



These results demonstrate a moderate level of unmet need for all patient groups.In the in-depth interviews, KOLs and payers were asked in more detail about their unmet needs.

Figure 2 and Figure 3 show the mean scores for unmet needs across gastroenterologists and nephrologists combined (n=18) and payers (n=17).

Figure 2: Unmet needs for IDA in IBD and IDA in CKD, according to KOLs (US& EU)

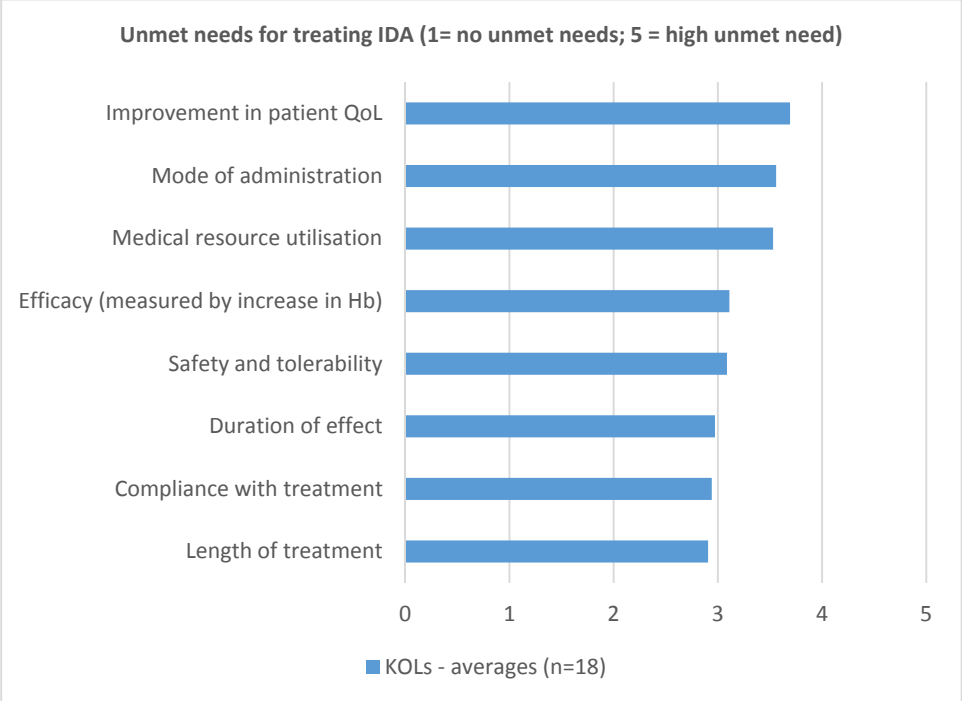
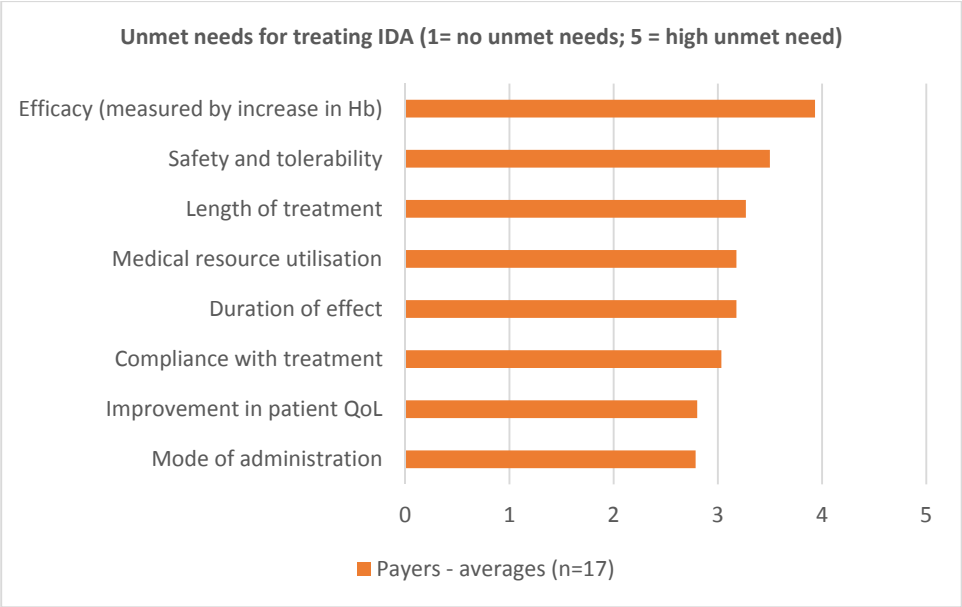


Figure 3: Unmet needs for IDA in IBD and IDA in CKD, according to payers (US& EU)



As can be seen, KOLs believe that the key unmet needs lie in improving patient quality of life and improving mode of administration and medical resource utilisation; these factors relate to IV iron treatments being expensive to administer, not only in terms of drug costs, but also the administration costs and time involved in doing so. Payers are concerned that they are getting an efficacious and safe medication.

There are some differences in the unmet needs for IBD patients, compared to CKD patients. IBD is a condition already associated with GI disturbances, so OFPs are often poorly tolerated. However, the alternative is not seen favourably as IV iron is costly.

"We need something that is absorbed, increases haemoglobin levels, makes the patient feel better, and has no side effects. This population often has bowel issues so iron can lead to flare ups." UK KOL, gastroenterologist

"It is difficult to have them [IBD patients] come in and receive infusions, it is better to be at home and they can do it themselves, like an oral, but with a better side-effect profile. This goes hand-in-hand with utilisation because the easier it is to use, the more it will be used. The existing oral products are not as effective which is why we do not use them, also side-effects like abdominal pain and constipation. If there was an oral that was effective as Venofer, I don't think I would even prescribe Venofer." US KOL, gastroenterologist

For patients with CKD, who receive dialysis in hospital, there is no issue with patients receiving IV iron at the time of dialysis, so for this group of patients, there were seen to be very few unmet needs. For pre-dialysis patients, a key unmet need is the high tablet burden that CKD patients are already under, and clinicians often prescribed IV iron for these patients as well as those undergoing dialysis.

"The reason we prefer IV to oral is adherence due to constipation and forgetfulness. Can you develop a pill that is once a week or once daily without GI side-effects? And that delivers an adequate dose of iron? We would also like something safer and more efficacious." US KOL, nephrologist

Iron therapy market

Market overview

Iron supplementation for the treatment of IDA can be achieved orally or intravenously.

Treatment with oral iron supplements is, in principle, simple, inexpensive, and effective way of treating iron deficiency conditions.[21] Ferrous sulphate is commonly available and inexpensive, but other oral iron preparations may also be used; there is not significant evidence to suggest that other oral iron formulations are more effective or associated with fewer adverse side effects than ferrous sulphate.[22] Other ferrous iron salts include fumarate, succinate and gluconate.

Unfortunately, existing oral iron formulations are a less than ideal treatment for many patients, mainly because of adverse events related to the gastrointestinal tract, lack of adherence to therapy or insufficient length of therapy for the degree of iron deficiency, poor duodenal absorption due to concomitant gastrointestinal pathologies (IBD or any other cause of chronic inflammation, malignancy) and the long course of treatment needed to resolve anaemia (1-2 months) and replenish body iron stores (another 3-6 months).[23] . Non-adherence to a prescribed course of oral iron is common and even in adherent patients, poor intestinal absorption fails to compensate for the iron need in the presence of ongoing blood losses or in inflammatory conditions.[24]

Ferrous sulphate is the current gold standard oral iron therapy. A systematic review and meta-analysis of randomised controlled trials (RCTs) confirmed that ferrous sulphate is associated with a significant increase in gastrointestinal (GI) specific side-effects versus placebo with an odds ratio (OR) of 2.32 [95%CI 1.74–3.08, p<0.0001, I2 = 53.6%] and versus IV iron with an OR of 3.05 [95%CI 2.07-4.48, p<0.0001, I2 = 41.6%]. Subgroup analysis in IBD patients showed a similar effect versus IV iron (OR = 3.14, 95% CI 1.34-7.36, p = 0.008, I2 = 0%).[25]

Treatment with IV iron presents several advantages over treatment with existing OFPs (due to their adverse event (AE) profile and poor absorpotion leading to lack of therapy adherence), such as faster and higher increase in Hb levels and replenishment of body iron stores.

There are a number of IV iron formulations available in the US and in Europe, as shown in Table 8. These include iron dextran, ferric gluconate and iron sucrose. In the last few years, several newer formulations have come onto the market, including ferric carboxymaltose (Ferinject/Injectafer) in the US and Europe, with iron isomaltoside 1000 (Monofer®) also being approved in Europe and Ferumoxytol (FeraHeme®/Rienso) in the US and EU (subsequently withdrawn in the EU 2015 due to safety reasons). In their pre-registration trials, all of these three new compounds potentially had better safety profiles than the more traditional IV preparations, these products may be given more rapidly and in larger doses than their predecessors with the possibility of complete replacement of iron in 15-60 minutes.

[21] Cançado RD1, Muñoz M. Intravenous iron therapy: how far have we come? Rev Bras Hematol Hemoter. 2011;33(6):461-9
[22] Kidney Disease: Improving Global Outcomes (KDIGO) Anemia Work Group. KDIGO Clinical Practice Guideline for Anemia in Chronic Kidney Disease. Kidney inter., Suppl. 2012; 2: 279–335.
[23] Cançado RD and Muñoz. Intravenous iron therapy: how far have we come? M Rev Bras Hematol Hemoter. 2011; 33(6): 461–469.
[24] Discussions with Key Opirion Leaders by GfK, July 2015
[25] Tolkien Z, Stecher L, Mander AP, Pereira DI, Powell JJ. Ferrous sulphate supplementation causes significant gastrointestinal side-effects in adults: a systematic review and meta-analysis. PLoS One. 2015 Feb 20;10(2)

It is worth noting that in 2013 the CHMP published new recommendations[26] to manage the risk of allergic reactions with IV iron-containing medicines. They concluded that **all** IV iron medicines have a small risk of causing allergic reactions, that can be life-threatening if not treated promptly.

Table 8: IV iron formulations available in US and Europe

Name	Brand	Administration/ Dose	Efficacy/Safety information
Low-molecular-weight iron dextran	INFeD®/ Cosmofer	Administered as an IV bolus or total dose infusion (TDI) with doses up to 1000 mg	Requires test dose. Potential for fatal anaphylactic reactions
High-molecular-weight iron dextran	Dexferrum® (US only)	Administered as an IV bolus or total dose infusion (TDI) with doses up to 1000 mg	Requires test dose. Potential for fatal anaphylactic reactions
Ferric gluconate (FG)	Ferrlecit	The maximum recommended dose is 125 mg given as a bolus or short infusion	A historical review of the use of FG in Europe and iron dextrans in the United States concluded that FG was a safer therapeutic option to iron dextran, associated with a lower risk of anaphylactoid reactions.[27]
Iron sucrose	Venofer	Administered as a 15-30 minute infusion in doses of 200-300 mg; the maximum weekly dose should not exceed 600 mg.	Efficacy and safety shown in the treatment of anaemia including in: - CKD patients on haemodialysis [28] [29] - IBD patients with IDA[30] Very low incidence of anaphylaxis (0.002%)
Ferric carboxymaltose	Ferinject/ Injectafer	Potential to administer large doses (15 mg/kg; maximum of 1000 mg/infusion) in a single and rapid (15-minute) infusion without the requirement of a test dose.	Lower risk of anaphylactic reaction Efficacy evaluated in several randomized, open-label, controlled, multicentre trials under different conditions associated with absolute or functional iron deficiency with or without anaemia, including patients with IBD, heavy uterine bleeding, postpartum IDA, chronic heart failure and CKD patients on haemodialysis or not. In clinical most drug-related AEs were

[26] European Medicines Agency. 28 June 2013. New Recommendations to Manage Risk of Allergic Reactions with Intravenous Iron Containing Medicines.
[27] Faich G, Strobos J. Sodium ferric gluconate complex in sucrose: safer intravenous iron therapy than iron dextrans. Am J Kidney Dis. 1999 Mar;33(3):464-70.
[28] Van Wyck DB1, Roppolo M, Martinez CO, Mazey RM, McMurray S; United States Iron Sucrose (Venofer) Clinical Trials Group. A randomized, controlled trial comparing IV iron sucrose to oral iron in anemic patients with nondialysis-dependent CKD. Kidney Int. 2005 Dec;68(6):2846-56.
[29] Critchley J, Dunbar Y. Adverse events associated with intravenous iron infusion (low-molecular weight iron dextran and iron sucrose): a systematic review. Transf Altern Transf Med. 2007; 9(1): 8-36
[30] Gasche C, Berstad A, Befrits R, Beglinger C, Dignass A, Erichsen K, et al. Guidelines on the diagnosis and management of iron deficiency and anemia in inflammatory bowel diseases. Inflamm Bowel Dis. 2007; 13(12): 1545-53

			considered transient and mild to moderate in intensity. Treatment was not permanently discontinued for any patient due to AEs. [31] [32] [33]
Ferumoxytol	FeraHeme® (now US only)	It can be administrated as a relatively large dose (max 510 mg) in a rapid (< 20 seconds) session without test dose requirement.	This formulation was approved by the FDA in 2009 for iron replenishment in CKD patients with IDA (withdrawn in EU due to safety reasons) Ferumoxytol administration may transiently interfere with diagnostic ability of magnetic resonance imaging which is frequently used for the diagnosis and follow-up of IBD; consequently this does not seem to be an appropriate IV iron compound for IBD patients. In 2015, a new boxed warning regarding the risk for serious hypersensitivity/ anaphylaxis reactions was added.
Iron isomaltoside 1000	Monofer (Europe only)	Administered as a rapid high dose infusion of up to 2000 mg without the application of a test dose	Efficacy demonstrated in several randomized open-label trials in patients with anaemia associated with IBD, CKD, and as maintenance therapy in HD patients, plus in trials for prevention of post-operative anaemia. Monitoring necessary for signs and symptoms of hypersensitivity reactions during and following each administration

The benefit of some of the newer IV formulations is that they can offer the efficacy of IV iron administration in fewer injections and shorter administration times. This can be associated with real cost-saving benefits for hospitals and healthcare providers (reduced visits, reduced physician and nurse time) and patients (less frequent and shorter hospital visits).[34]

[31] Ferinject Summary of Product Characteristics, las revised October 2014.
[32] Anker SD, Comin Colet J, Filippatos G, Willenheimer R, Dickstein K, Drexler H, Lüscher TF, Bart B, Banasiak W, Niegowska J, Kirwan BA, Mori C, von Eisenhart Rothe B, Pocock SJ, Poole-Wilson PA, Ponikowski P, FAIR-HF Trial Investigators Ferric carboxymaltose in patients with heart failure and iron deficiency. N Engl J Med. 2009; 361(25): 2436-48 Comment in: N Engl J Med. 2009;361 (25):2475-7. Ann Intern Med. 2010;152(8):JC4-5
[33] Van Wyck DB, Mangione A, Morrison J, Hadley PE, Jehle JA, Goodnough LT. Large-dose intravenous ferric carboxymaltose injection for iron deficiency anemia in heavy uterine bleeding: a randomized controlled trial. Transfusion. 2009; 49(12): 2719-28
[34] GfK discussions with clinicians and payers. July 2015

Guidelines for IDA in CKD

There are numerous guidelines for the treatment of IDA in patients with CKD, at a national and international level.

- In the UK the Renal Association,[35] Royal College of Physicians[36] and NICE[37] have guidelines for Anaemia Management in Chronic Kidney Disease
- In Europe, the Anaemia Working group of European Renal Best Practice (ERBP) have published a position statement for Anaemia Management in Patients with CKD[38]
- In the US, the National Kidney Foundation publish the Kidney Disease Outcomes Quality Initiative (KDOQI) Guidelines for management of anaemia in CKD[39]
- Kidney Disease: Improving Global Outcomes (KDIGO) Clinical Practice Guideline for Anemia in Chronic Kidney Disease is an international guideline[40]

Whilst there are variations in practice amongst clinicians, and treatment algorithms vary between institutions depending on the needs of individual patients and available resources, there are broad recommendations in the treatment of patients with IDA and CKD that can be generalised. The KDIGO guidelines on treatment choice of iron replacement therapy are outlined in Figure 4.

[35] Mikhail A, Shrivastava R, Richardson D. Anaemia in CKD. 15 November 2010
[36] National Collaborating Centre for Chronic Conditions. Anaemia management in chronic kidney disease: national clinical guideline for management in adults and children. London: Royal College of Physicians, 2006.
[37] NICE Guidelines [NG8] Anaemia Management in people with chronic kidney disease. June 2015
[38] Locatelli F, Covic A, Eckardt KU, Wiecek A, Vanholder R, and on behalf of the ERA-EDTA ERBP Advisory Board. Anaemia management in patients with chronic kidney disease: a position statement by the Anaemia Working Group of European Renal Best Practice (ERBP). Nephrol. Dial. Transplant. (2009) 24 (2): 348-354
[39] National Kidney Foundation. KDOQI Clinical Practice Guidelines and Clinical Practice Recommendations for Anemia in Chronic Kidney Disease. Am J Kidney Dis 47:S1-S146, 2006 (suppl 3). And Update (2007) of Hemoglobin Target
[40] Kidney Disease: Improving Global Outcomes (KDIGO) Anemia Work Group. KDIGO Clinical Practice Guideline for Anemia in Chronic Kidney Disease. Kidney inter., Suppl. 2012; 2: 279–335

Figure 4: KDIGO guidelines on the use of iron to treat anaemia in CKD

2.1.1: When prescribing iron therapy, balance the potential benefits of avoiding or minimizing blood transfusions, ESA therapy, and anemia-related symptoms against the risks of harm in individual patients (e.g., anaphylactoid and other acute reactions, unknown long-term risks).

2.1.2: For adult CKD patients with anemia not on iron or ESA therapy we suggest a trial of IV iron (or in CKD ND patients alternatively a 1–3 month trial of oral iron therapy) if:

- **an increase in Hb concentration without starting ESA treatment is desired* and**
- **TSAT is r30% and ferritin is r500 ng/ml (r500 mg/l)**

2.1.3: For adult CKD patients on ESA therapy who are not receiving iron supplementation, we suggest a trial of IV iron (or in CKD ND patients alternatively a 1–3 month trial of oral iron therapy) if:

- **an increase in Hb concentration or a decrease in ESA dose is desired** and**
- **TSAT is r30% and ferritin is r500 ng/ml (r500 mg/l)**

2.1.4: For CKD ND patients who require iron supplementation, select the route of iron administration based on the severity of iron deficiency, availability of venous access, response to prior oral iron therapy, side effects with prior oral or IV iron therapy, patient adherence, and cost.

2.1.5: Guide subsequent iron administration in CKD patients based on Hb responses to recent iron therapy, as well as ongoing blood losses, iron status tests (TSAT and ferritin), Hb concentration, ESA responsiveness and ESA dose in ESA treated patients, trends in each parameter, and the patient's clinical status.

2.1.6: For all pediatric CKD patients with anemia not on iron or ESA therapy, we recommend oral iron (or IV iron in CKD HD patients) administration when TSAT is r20% and ferritin is r100 ng/ml (r100 lg/l).

2.1.7: For all pediatric CKD patients on ESA therapy who are not receiving iron supplementation, we recommend oral iron (or IV iron in CKD HD patients) administration to maintain TSAT 420% and ferritin 4100 ng/ml (4100 lg/l).

*Based on patient symptoms and overall clinical goals, including avoidance of transfusion, improvement in anemia-related symptoms, and after exclusion of active infection.

**Based on patient symptoms and overall clinical goals including avoidance of transfusion and improvement in anaemia-related symptoms, and after exclusion of active infection and other causes of ESA hyporesponsiveness.

Guidelines for IDA in IBD

The European Crohn's and Colitis Organisation (ECCO) have published a European Consensus on the Diagnosis and Management of Iron Deficiency and Anaemia in Inflammatory Bowel Disease.[41]

In these guidelines, the route of administration for iron supplementation is considered, as shown in Figure 5.

[41] Dignass AU et al. European Consensus on the Diagnosis and Management of Iron Deficiency and Anaemia in Inflammatory Bowel Disease. J Crohn's and Colitis, 2015, 1-12

Figure 5: ECCO guidelines on the route of administration of iron supplementation in IBD patients

3.2.1 ECCO Anaemia Statement 2C

Intravenous iron should be considered as first line treatment in patients with clinically active IBD, with previous intolreance to oral iron, with hemoglobin below 10g/dL, and in patients who need erythropoiesis-stimulating agents [ESAs]

3.2.3 ECCO Anaemia statement 2E

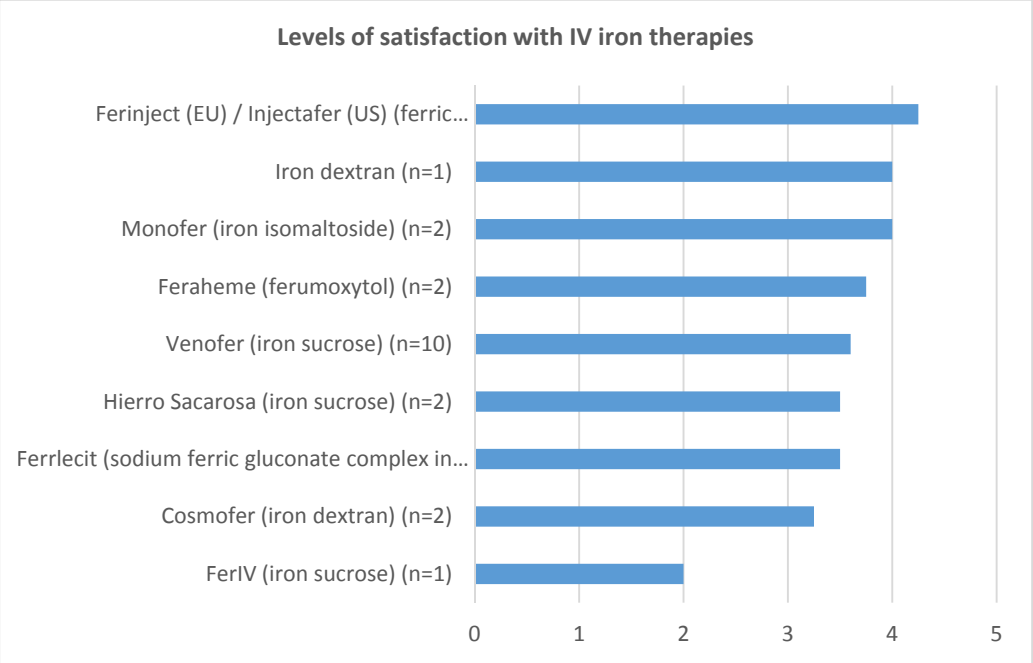
Oral iron is effective in patients with IBD and may be used in patients with mild anaemia, whose disease is clinically inactive, and who have not been previously intolerant to oral iron.

These guidelines mention ferric maltol as having preliminary data which indicate effectiveness with a preferred adverse event profile, even in IBD patients with a history of intolerance to ferrous sulphate.[42]

Perception of therapy options

Based on responses from the TDIs, current treatment options are viewed by the KOLs and clinicians as being moderately satisfactory. Gastroenterologists and nephrologists had similar levels of satisfaction with each of the products and the average level of satisfaction for each of the products is shown in Figure 6.

Figure 6: Level of satisfaction amongst Gastroenterologists and Nephrologists with IV iron therapies (US&EU)



Level of satisfaction was scored between 1 to 5 (1=unsatisfied with treatment to 5=completely satisfied with treatment)

[42] Dignass AU et al. European Consensus on the Diagnosis and Management of Iron Deficiency and Anaemia in Inflammatory Bowel Disease. J Crohn's and Colitis, 2015, 1-12

In the online survey, GfK asked gastroenterologists and nephrologists about their use of IV iron, and the results are shown in Figure 7 and Figure 8.

Figure 7: IV iron allocation amongst gastroenterologists in EU3 and US, for treatment of IDA

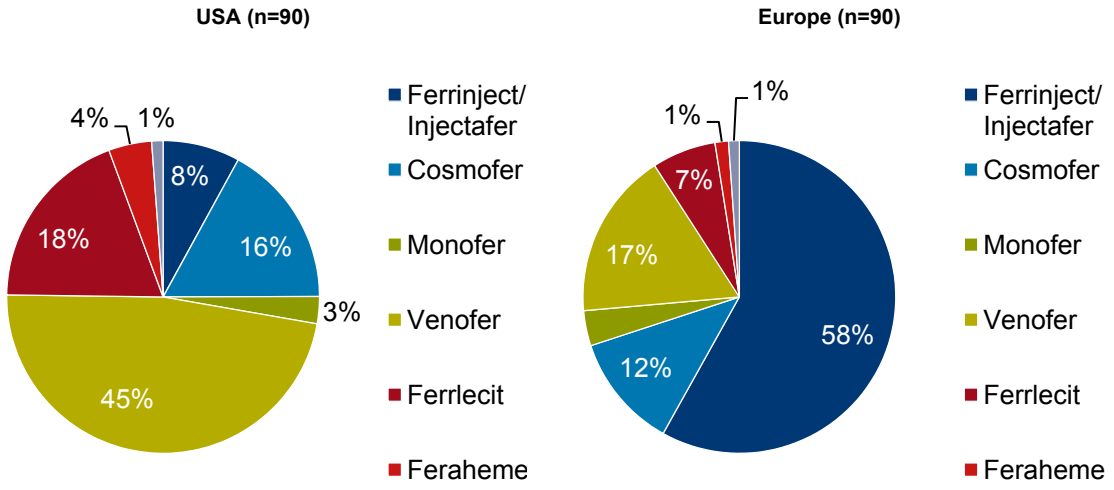
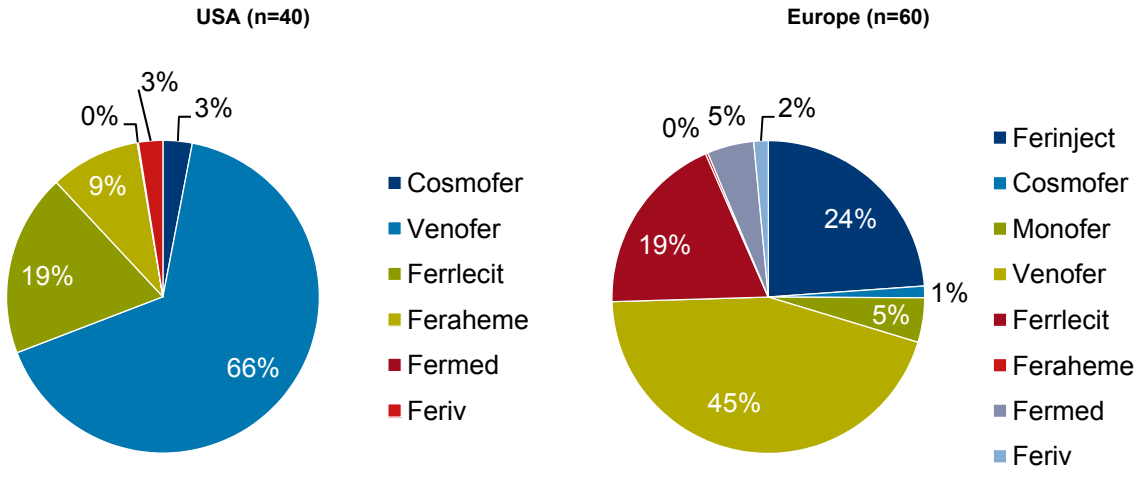


Figure 8: IV iron allocation amongst nephrologists in EU3 and US, for treatment of IDA



Ferinject/Injectafer and Venofer are the most widely used IV iron products, and with its superior dosing schedule, respondents were most satisfied with Ferinject. With Venofer there were concerns over the number of visits a patient had to make within a short period of time to receive the product.

"We use mostly Ferinject because it is well-tolerated and very effective in regards of fast onset; you get iron saturation levels within very short times" German KOL, gastroenterology

The main downside mentioned for the IV products, was the cost of treatment associated with having to give patients infusions, and inconvenience for patients.

"I have to bring patients in frequently for infusions. It's expensive, I have to book an infusion suite and cost is therefore an issue. Anything that brings costs down would be good. It's not just a cost for the hospital as well - there is the cost of the patient time and parking at the hospital for 4 hours, which can be stressful for the patient." UK KOL, Gastroenterologist

There would therefore appear to be a need for an effective iron product, with few adverse events, that is not administered through the IV route.

Feraccru and its place in the market

Description

Feraccru, ferric maltol [3-hydroxy-2-methyl-4H-pyrane-4-one iron (III) complex (3:1)] (INN: ferric maltol), is a new, chemically stable complex (chelate) of ferric iron and maltol.

Feraccru is an iron replacement preparation. Its anatomical therapeutic classification (ATC) pharmaco-therapeutic group is iron trivalent, oral preparation; the ATC code is BO3AB (not yet assigned at the 6th level).

Feraccru is indicated for the treatment of adults with iron deficiency anaemia (IDA) in patients with inflammatory bowel disease (IBD).Feraccru is administered twice daily (i.e. morning and evening), swallowed on an empty stomach with water.

Competitive position

The multicentre Phase III clinical trial for Feraccru versus placebo demonstrates the therapeutic benefit of Feraccru. Adult patients with quiescent or mild-to-moderate ulcerative colitis or Crohn's disease, mild-to-moderate IDA (9.5 – 12.0 g/dL/9.5 – 13.0 g/dL in females/males, respectively) and documented failure on previous OFP received oral Feraccru capsules (30mg b.i.d.) or identical placebo for 12 weeks according to a randomized, double-blind, placebo-controlled study design. This study was carried out in 128 patients. Significant improvements in Hb were observed with Feraccru versus placebo at Weeks 4, 8 and 12 and Hb was normalised in two-thirds of patients by Week 12. Clinically relevant haemoglobin (Hb) increase is considered to be 1g/dL. In the trial, Feraccru delivered a 2.3g/dL rise within 12 weeks, achieving a 1g/dL rise in only 4 weeks.

The safety of Feraccru was comparable with placebo, with no impact on disease severity, with good adherence levels (>90%).

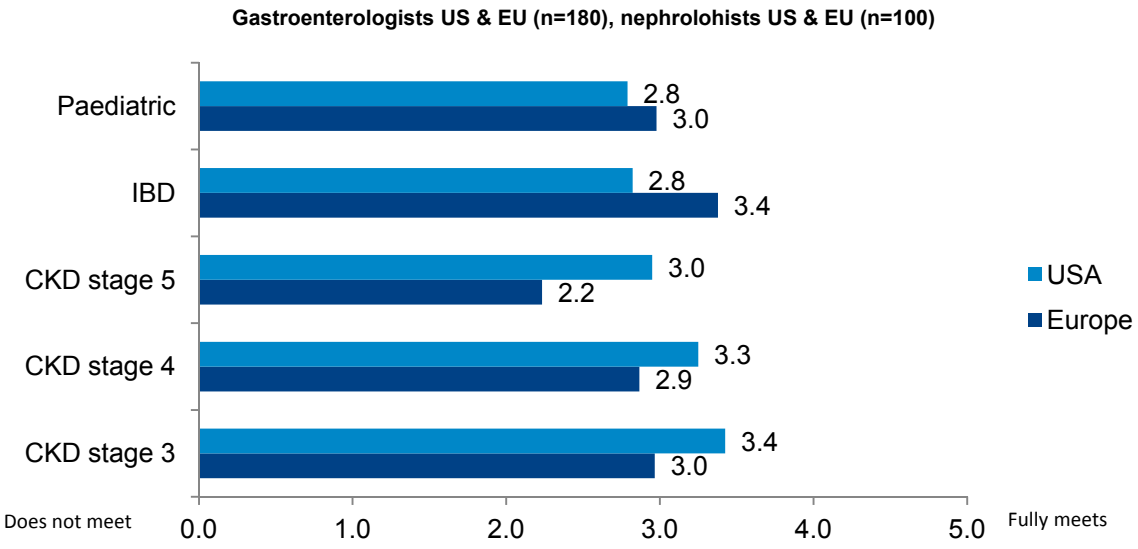
Feraccru, is therefore, able to address a number of the unmet needs associated with current iron therapies:

- Readily absorbed with few side effects
- Provides rapid IV-like improvements in haemoglobin (Hb) levels
- Chronic therapy with Feraccru appears to remove the need for further IV iron

In the online survey, gastroenterologists (n=180) and nephrologists (n=100) were asked to score, on a scale of 1 to 5, how well Feraccru met the unmet needs for each patient group they treated. A score of 1 meant that Feraccru did not meet the unmet needs, and a score of 5 meant that Feraccru fully met the unmet needs for that group of patients. Respondents were presented with the scenario

that Feraccru had clinical data showing it was superior to placebo. The outputs from this research, which are shown in Figure 9, demonstrate that in Europe IBD patients were seen as being the patients who would most benefit from Feraccru. These patients are in need of an oral treatment with a more favourable GI side effect profile. Likewise, the paediatric population do not like IV treatments, so an oral treatment would be of benefit in this group of patients.

Figure 9: Ability of Feraccru to meet unmet needs associated with current IDA treatments



Within the CKD patient population, Feraccru was seen as having least value for CKD Stage 5 patients, as they have regular dialysis, and receive IV iron treatment at the same time. There is more value for patients with CKD Stage 3, who are pre-dialysis – this was most prominent amongst US respondents.

Introduction of Feraccru TPPs (X1, X2, X3)

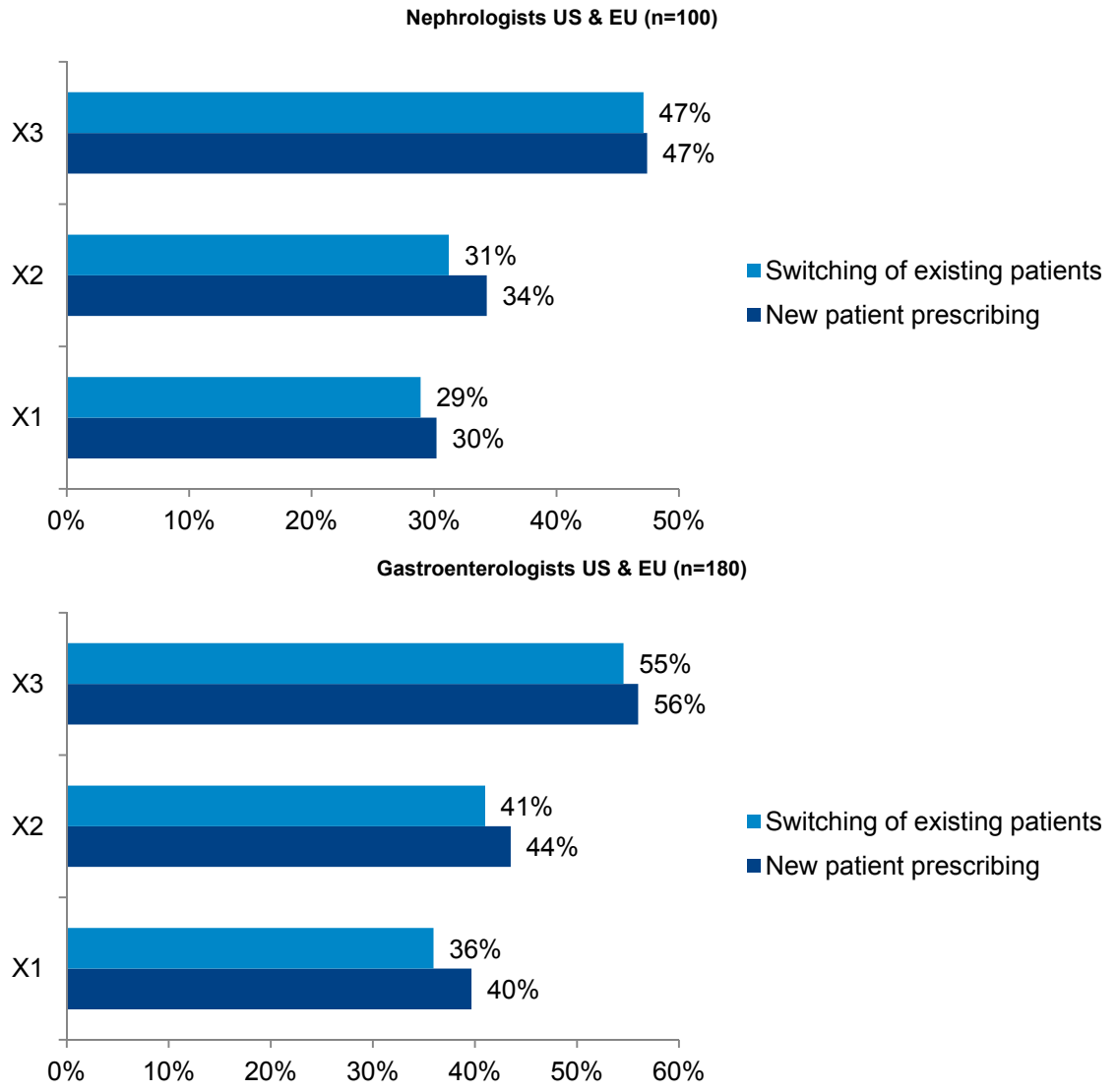
Clinicians were asked to what proportion of new patients they were likely to prescribe Feraccru, given different scenarios.

- Scenario X1: Feraccru is shown to be superior to placebo
- Scenario X2: Feraccru is shown to be non-inferior to IV iron (a clinical trial vs. IV iron is planned)
- Scenario X3: Feraccru is shown to be superior to IV iron

In GfK's view, only scenarios X1 and X2 are pertinent in the context of Feraccru. Scenario X3 was included as part of the research design in order to test respondent sensitivity and in the context of Feraccru, GfK considers it would be unnecessary for a company to demonstrate superiority vs IV iron. Clinicians were then asked to score their level of interest, and again what percentage of new patients they would prescribe Feraccru. Given this additional data gastroenterologists (across US/EU) stated that they would consider prescribing between 40-56% of their new patients and between 36-55% of their switch patients to Feraccru based on the TPPs presented. Nephrologists indicated that they would prescribe between 30-47% of their new patients and 29-47% of their switch patients to Feraccru based on the TPPs presented.

The mean scores for both groups (nephrologists and gastroenterologists) increased with data vs. IV iron available, indicating that clinicians were more likely to prescribe new patients with Feraccru and switch more patients to Feraccru.

Figure 10: New patient prescribing of, and switching of existing patients to, Feraccru under scenarios X1, X2, and X3



"I would prescribe this new product [Feraccru with non-inferiority data to IV iron] systematically to all patients requiring iron IV, not just on patients where I would suspect an adherence issue." Spanish KOL, nephrologist

Products in Development

The majority of clinicians believed that Feraccru was able to offer benefits over existing treatments, namely it is an oral treatment, which is effective, and has few adverse events associated with it.

Discussions with gastroenterologists, nephrologists and payers, along with a commercial pipeline database[43] search, has revealed that there are few products in development to treat IDA.

Soluble ferric pyrophosphate (SFP) for the treatment or prevention of iron deficiency anaemia in patients undergoing haemodialysis for chronic kidney disease or end-stage renal disease (ESRD), developed by Rockwell Medical Technologies.The product is administered via dialysate and contains FePPi (ferric pyrophosphate), a highly stable, water-soluble, non-polymeric, simple iron salt that does not require processing by the liver. When used in haemodialysis, it crosses the dialyzer membrane to enter the bloodstream, is bound by apotransferrin and transferred to the bone marrow. The dialysate mode of administration, directly into the bloodstream through slow infusion, avoids toxicity and overcomes the need for iron release from reticuloendothelial stores in the liver and other organs. Studies have shown that soluble ferric pyrophosphate product did not oversaturate transferrin and preserved plasma unsaturated iron binding capacity. Also, the product was found to reduce the use of erythropoietin-stimulating agent. This product was launched in the US in September 2015 (under the name Triferic). , and Phase III development is underway in Canada and Puerto Rico. Rockwell is also conducting phase I trials of intravenous (total parenteral nutrition, TPN) and oral formulations of SFP, as well as in patients undergoing peritoneal dialysis.

NOX-H94 (Lexaptepid Pegol) is an anti-Hepcidin Spiegelmer being developed for treatment of anaemia of chronic disease, a type of anaemia resulting from dysregulation of internal iron stores. Hepcidin is a peptide hormone which is known to directly trigger degradation of the cellular channel through which iron is exported from storage cells, and thus reduces available iron in the blood for haemoglobin production. Over time, this results in a form of anaemia which is poorly responsive to erythropoiesis-stimulating agents (ESAs). NOX-H94 completed a pharmacodynamic study in healthy volunteers challenged with endotoxin demonstrating its ability to block hepcidin-mediated effects on serum iron levels. A Phase IIa pilot study with NOX-H94 was conducted in 12 anaemic cancer patients. Five of the twelve patients (or 42%) reached the target haemoglobin level increase of ≥1 g/dL in response to NOX-H94 monotherapy and were qualified as "responders". In addition, the study identified diagnostic markers that will guide selection of patient populations in future studies in this indication.

Several interviewees mentioned recent publications and ongoing research into the role that iron supplementation plays in adversely affecting gut microbiota, [44] [45] and this may become more important in the future when considering iron supplementation of certain individuals.

Development status and plans for Feraccru

A series of clinical studies (over the last two decades) with Feraccru in healthy subjects and in anaemic patients (with and without IBD), although not conducted to current standards of GCP, has

[43] ADIS Insight – R&D Insight. Accessed 5th January 2016
[44] Gut 2015;64:696-697
[45] Kortman GA, Raffatellu M, Swinkels DW, Tjalsma H Nutritional iron turned inside out: intestinal stress from a gut microbial perspective. FEMS Microbiol Rev. 2014 Nov;38(6):1202-34.

provided a considerable body of knowledge on the absorption, efficacy, safety and tolerability of a range of doses of Feraccru.

A clinical development programme was established to provide pivotal registration data to support the marketing authorisation approval (MAA) for Feraccru. This programme included two PK studies (one a sub-study) and a pivotal Phase III efficacy and safety study (conducted as two separate protocols in ulcerative colitis (UC) and Crohn's disease (CD) patients respectively) that were fully adherent with good clinical practice (GCP).

Study ST10-01-101 was an open-label, randomised, multiple dose PK study conducted with 24 subjects with iron deficiency (with or without anaemia). The primary objective of Study ST10-01-101 was to evaluate the kinetics of maltol along with its metabolite, maltol glucuronide, as well as iron uptake in blood and urine after single and repeated bid oral doses of 30 mg, 60 mg or 90 mg Feraccru for 7 days, followed by a final dose on the morning of day 8.

Study ST10-01-102 was a prospective PK sub-study of subjects receiving Feraccru 30 mg bid in the open-label phase of studies ST10-01-301 or ST10-01-302. The objective of ST10-01-102 was to describe the PK profile of Feraccru at steady state after a 30 mg single dose in the target patient population, i.e. patients with IDA and IBD.

The pivotal, phase III, multicentre, randomised, double-blind, placebo-controlled study with Feraccru for the treatment of IDA in subjects with IBD where OFP had failed or could not be used, was conducted via two separate protocols:

- ST10-01-301 (AEGIS 1) in patients with quiescent ulcerative colitis (UC)
- ST10-01-302 (AEGIS 2) in patients with quiescent Crohn's disease (CD)

The study designs for these protocols were essentially identical except for the differing IBD population.

Efficacy was evaluated over the first 12 weeks of randomised treatment. All completed subjects from the randomised phase received open-label Feraccru for up to an additional 52 weeks, with the exception of patients recruited in Austria, where the Ethics Committee would not sanction the 52-week extension of the study unless the sponsor agreed to un-blind patients after the initial 12-week placebo period of the protocol. The sponsor was unwilling to agree to this.

Following regulatory agency agreement that the analysis of a single combined dataset from both studies would be scientifically and statistically valid, the analysis plan was integrated. In addition, in response to requests from the rapporteur and co-rapporteur, the dataset has been reanalysed for the primary efficacy endpoint, within each protocol dataset ([Feraccru-01-301 and Feraccru-01-302] according to the IBD diagnosis). An interim safety analysis of the open-label phase (cut-off date 31st March 2014) has been performed.

The rationale for the placebo-controlled protocols rather than comparative trials is primarily for the following reasons:

- A comparative study with ferrous products would likely lead to most of the control patients already intolerant of such products, dropping out as a result of intolerance or non-adherence, threatening the integrity of the study

- A double-blind IV-controlled study was considered, but following a prospective review by some investigators and ethics committees it was decided it would not be possible without including a placebo IV infusion arm, which was considered unethical

The Applicant obtained advice on design of Phase III studies and clinical development from BfArM and MHRA. Specific questions on the acceptability of the endpoints (see M2.7.3.2) proposed in the Phase III studies and the proposed number of patients that would be exposed to Feraccru for 6 and 12 months were proposed. Additional advice was sought from these agencies on the scientific and statistical validity of the analysis of a single combined dataset from both studies and the acceptability of filing on the basis of this single pivotal data set. The formal advice documents from these agencies and pre-submission meetings with BfArM and AEMPS are located in M5.4 - MHRA Meeting Minutes, 2010; MHRA Meeting Minutes, 2011; BfArM Meeting Minutes and AEMPS Meeting Minutes.

Supportive evidence for the efficacy of Feraccru in patients from IDA is provided by further published and unpublished studies.

Shield Therapeutics plans to conduct some additional Phase III studies:

- Phase IIIb study in patients with IDA-IBD, comparing Feraccru to an IV iron comparator
- Phase IIIa study in patients with IDA-CKD

Clinical development plans include studies to support launch into the paediatric market, and a paediatric plan has been agreed with EU regulators, and has been published.

To additionally support commercialisation of Feraccru the Company has commenced a head-to-head study of Feraccru versus IV iron with the following design features:

- a non-inferiority design with a significant delta of +/- 0.5g/dL of haemoglobin; a significant number of subjects (~240) to reduce the risk of statistical anomalies,
- a duration of treatment with Feraccru that previous studies demonstrate delivers the majority of the improvement in haemoglobin that Feraccru provides;
- two either/or primary endpoints; a cohort of subjects - anaemic IBD patients - in whom Feraccru has already demonstrated unequivocal effectiveness;
- a cohort of subjects who are more anaemic than those in the already completed phase 3 development of Feraccru that recognises more anaemic patients have a greater response to therapy;
- a primary endpoint that requires a smaller increase in haemoglobin that that seen in the AEGIS phase 3 programme.

If these end-points are achieved, they will further support the claim that Feraccru can be used in preference to IV iron infusions in the targeted patient cohorts.

Regulatory status and plans

In the European Union, the Marketing Authorisation Application (MAA) for Feraccru was filed via the centralised procedure on 1st December 2014. A positive opinion was adopted by the Committee for

Medicinal Products for Human Use (CHMP) in December 2015 and the EU commission decision (marketing authorisation) is expected in Q1 2016 which will allow EU-wide commercialisation of Feraccru.

Prior to MAA filing, Shield Therapeutics undertook a series of interactions with regulatory agencies (beginning in September 2010) which enabled Feraccru to benefit from an accelerated regulatory pathway, as confirmed by dialogue with Regulatory Agencies.

Interactions have been held with Regulatory Agencies in the UK, Germany and Spain.

In the US, Shield Therapeutics has had interactions with the FDA. At the pre-IND meeting, the Chemistry Manufacturing Controls (CMC) data package to support the Phase III study in CKD and NDA was discussed, along with the design of the Phase III study in CKD patients. Also discussed was the acceptability of the existing non-clinical data package to support an MAA, and the extent of clinical data to support NDA. The outcomes of this meeting were that a CMC package for IND was agreed, FDA input on the proposed CKD protocol was obtained (in terms of the primary endpoint), it was confirmed that the non-clinical package was acceptable, and FDA agreement was obtained that GCP pharmacokinetic data was not required for Phase III.

It is planned that following EU approval, other market launches will follow through with the use of local regulatory expertise through partnering process or local CROs/distributors.

Table 9: Country regulatory landscapes

Country	Comments
First wave with accelerated procedures referring to EU approval: e.g. Turkey, Switzerland, Australia/New Zealand	Usually need local registered entity/responsible pharmacist
CADREAC countries: Bulgaria/Croatia/Romania	Acknowledge EU MAA – 4-5m process
Second wave countries, e.g. Serbia and other Balkan states; Israel, North/East Africa, Middle East, Asia, Russia and CIS	In many countries approval based on CPP from country of origin (UK/EU); Local agent/responsible pharmacist
Japan	eCTD and full assessment May need local bridging study

CADREAC = Collaboration Agreement of Drug Regulatory Authorities in European Union Associated Countries

CPP = Certificate of Pharmaceutical Product

eCTD = electronic Common Technical Document

CIS = Commonwealth of Independent States

Manufacturing status and plans

Shield Therapeutics has a long term relationship with Piramal Healthcare (UK) Ltd ("Piramal"), a contract manufacturer, who is contracted to produce sufficient commercial batches of Feraccru in time for planned launch. Piramal offers full cGMP development and manufacturing, with integrated services across the pharmaceutical supply chain, drug substance, drug product manufacturing, clinical trials packaging, distribution, and commercial supply. They are a US FDA and UK MHRA approved facility.

To Q4 2010, Piramal manufactured 3 batches of drug substance (8-15kg), and 2 batches of drug product of 15,000 and 65,000 capsules.

Since then, clinical trial drug product has been manufactured to specification at a volume of 120,000 capsules per batch.

In preparation for launch, various Chemistry Manufacturing Controls (CMC) have been put in place. These include preparing to scale up by ten times, in line with the MAA submission limits. Drug substance batches of 240-280kg, and drug product capsules up to 1,200,000 batches. Shield Therapeutics aims to produce 3,500,000 for initial launch which will guarantee 4,800 patients a yearly supply.

Shield Therapeutics plans to approve an alternative supplier of the raw materials, and identify a second supplier for Feraccru post launch in order to secure supply.

Market potential

According to data from IMS Midas, the global market for iron products, as of Q3, 2014 was c. £1.6 billion, and is growing. The IV iron market by itself is c. £600 million.[46]

Feraccru has the potential to take share in the iron products market, through prescribing of Feraccru to patients who have recently failed on OFPs ("new" patients) and to patients who have already tried IV iron, but who will be switched onto Feraccru ("switch" patients).

GfK, in the online survey and in the in-depth telephone interview programme, asked gastroenterologists and nephrologists about their likelihood to prescribe Feraccru to new patients, along with their likelihood to prescribe Feraccru to patients receiving intermittent IV therapy. In the following charts (Figure 11 and Figure 12) responses are based on Feraccru only having data showing it is superior to placebo.

"It is very promising in terms of iron increase, efficacy in normalizing haemoglobin, and reducing side-effects. It is quite superior to what we have today." Spanish KOL, gastroenterologist

Clinicians (both gastroenterologists and nephrologists) in the US demonstrate a higher willingness to prescribe Feraccru to new and switch patients than those in Europe. Overall, gastroenterologists were more willing to prescribe Feraccru to their new and switch patients than were nephrologists. This was expected as IV iron is an acceptable product for CKD patients on dialysis.

[46] Galenica Annual Report 2014

Figure 11: Willingness of clinicians to prescribe Feraccru to new patients and switch existing patients (based on Feraccru demonstrating superiority vs. placebo data only)

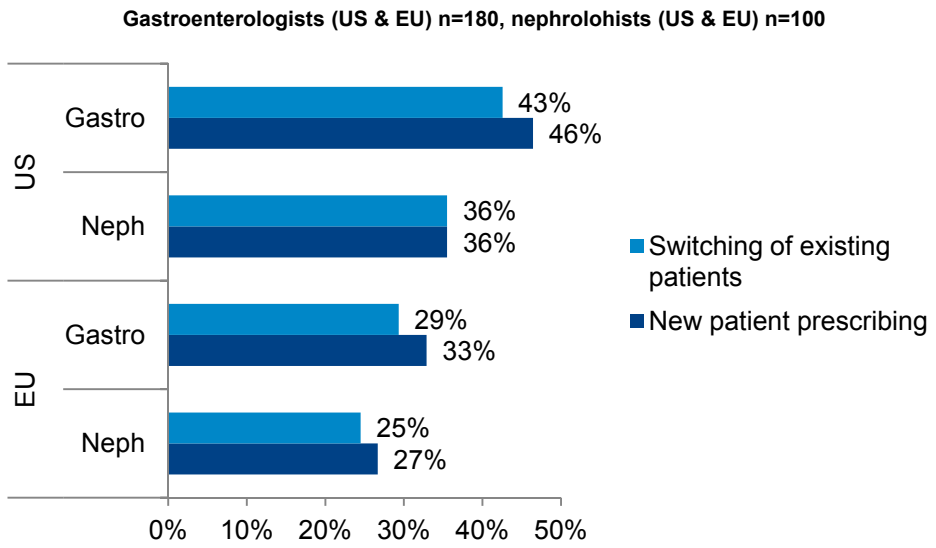
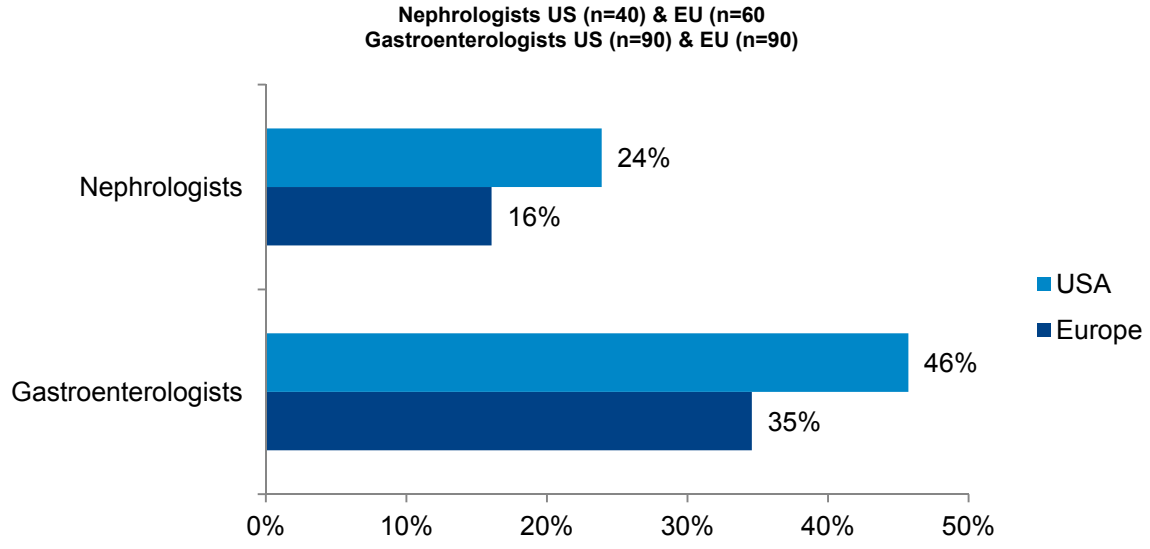


Figure 12 shows the willingness of clinicians to switch patients who are receiving intermittent IV therapy to Feraccru. Again, the US clinicians have a higher willingness to prescribe than European clinicians, and in this case, gastroenterologists are more likely to switch IBD patients to an oral product than nephrologists are to switch CKD patients. This is to be expected, as nephrologists often expressed that, for patients on dialysis, IV iron was an acceptable product, and this question did not differentiate between those patients on dialysis and patients not on dialysis.

Figure 12: Willingness of clinicians to switch patients from intermittent IV treatment to Feraccru (based on Feraccru demonstrating superiority vs. placebo data only)



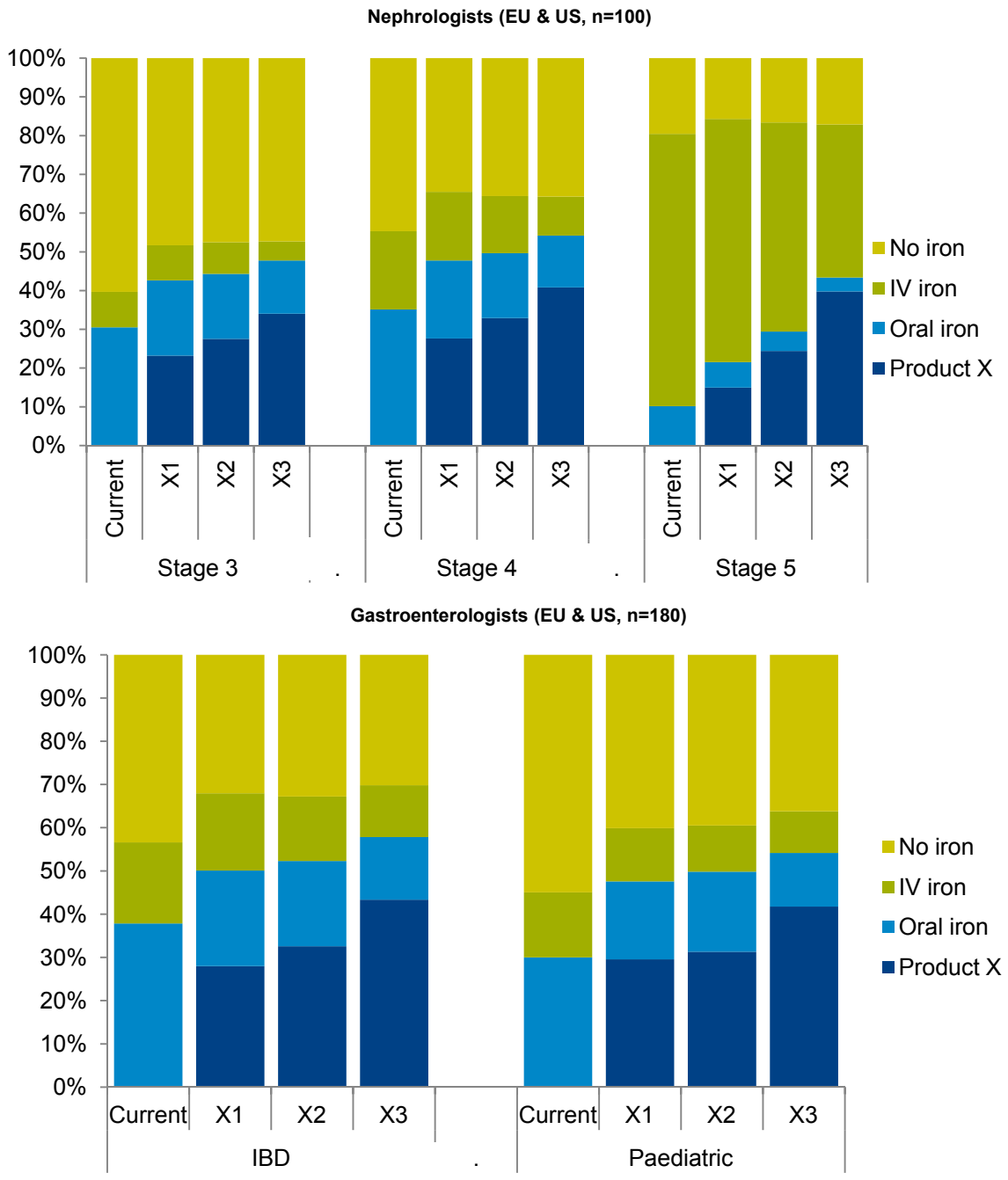
If Feraccru is able to show in trials that it is non-inferior to IV iron, then it can be expected that Feraccru will achieve a higher share, as clinicians show a greater willingness to prescribe, as

demonstrated in Figure 13. In this figure, the scenarios presented for Feraccru were that X1 is superior to placebo, X2 is non-inferior to IV iron and X3 is superior to IV iron.

"Nearly all my patients would be candidates to Product X2 as it is equal or better than existing molecules and is administered orally." Spanish KOL, gastroenterologist

Figure 13 demonstrates that the allocation of Feraccru increases incrementally across all TPPs presented (X1, X2, X3). Higher sensitivity was shown in TPPs including a head-to-head comparison against IV iron. In scenario X1, Feraccru is allocated primarily to patients currently receiving no iron supplementation, resulting in market expansion. In scenarios X2 and X3, the incremental gain in allocation is derived primarily from competitor oral iron products. In scenarios X1 and X2, IV iron allocation remains stable, but in scenario X3 (superiority to IV iron) IV iron is to some extent substituted by Feraccru.

Figure 13: Iron supplement respondent allocation in CKD in the current market, and in scenarios X1, X2, and X3



If Shield Therapeutics does not achieve the head to head data demonstrating non-inferiority for Feraccru vs. IV iron, then the company will have to ensure that this data is presented in such a way so as not to impact too heavily on uptake.

Shield Therapeutics also needs to ensure that the timelines for recruitment and training of its sales force are met, in order to meet peak sales forecasts and timings.

Plans for commercialisation and achievements to date

Shield Therapeutics plans to sell Feraccru into the specialty care environment, with peer-reviewed data to achieve a change in the treatment guidelines, so that, in time, Feraccru is used in preference to IV iron in OFP intolerant patients.

Shield Therapeutics plans a phased roll-out, initially targeting the price-taking markets.

Shield Therapeutics will establish key operations in the UK, Germany, France, Spain and Italy; also covering affiliate territories such as Ireland, Benelux and Portugal. There will be phased recruitment of an initial field force of approximately 60 highly experienced Medical Science Liaison and hospital-based sales representatives to support and promote the use of Feraccru across these key EU territories. The size of this team will increase organically to meet demand to up to150 representatives.

Initially, gastrointestinal (GI) Consultants will be the focus, as they care for the IBD patients who have IDA, with the target patient group being IDA in IBD-anaemia and the oral ferrous intolerant patients. Shield Therapeutics will initially target switch patients (i.e. those who are currently on IV therapy) and will expand this over time to include all patients with IDA in the chosen indications. The EU label will be expanded as additional clinical data is produced, e.g. CKD/CHF.

US launch is anticipated in the two key indications of IBD and CKD.

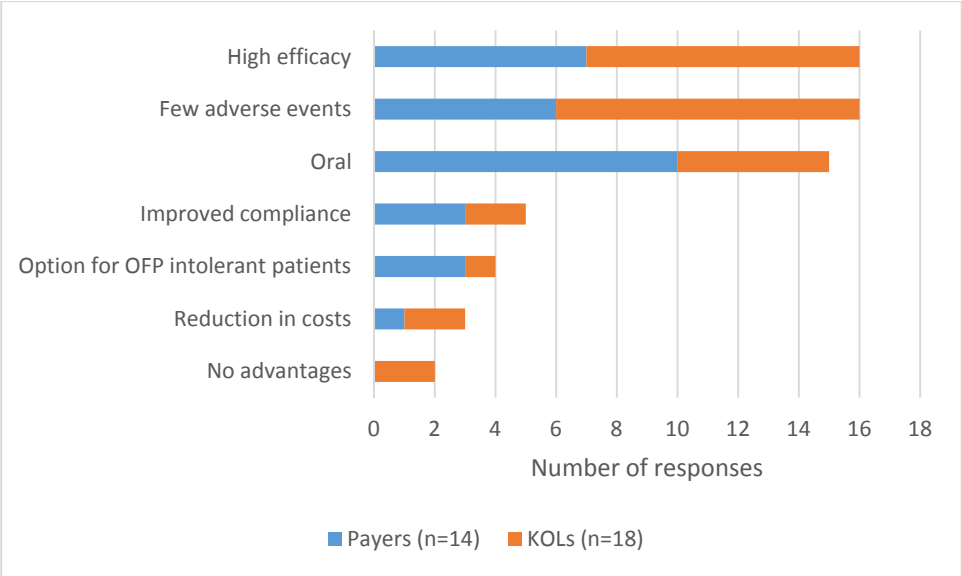
US commercialisation strategy will follow the same EU infrastructure plans and seek to gain from learnings in the EU launch to optimise the US plans.

US commercialisation plans will broadly follow the same EU infrastructure costs and plan is to initiate launch in US in 2019.

Product merits

Based on conversations with payers and KOLs, there are a number of features of Feraccru which were seen favourably. Respondents were asked to list advantages of Feraccru based on the product profile, and Figure 14 shows that an effective, oral iron replacement product, with few adverse events are the key advantages of Feraccru.

Figure 14: Perceived advantages of Feraccru amongst KOLs and Payers



"It [Feraccru] is one step further [than current OFPs] – we would be able to give oral a try first – and if it doesn't work we are able to give IV." German KOL, nephrologist

The study design (Feraccru vs. placebo) was seen as adequate, but respondents preferred the data showing Feraccru was non-inferior to IV, as it would be used in a broader patient population.

Key risks

There are a number of risks associated with conducting a Phase III trial of Feraccru vs. an IV comparator, which must be balanced with the potential upside of a favourable outcome of such a trial.

A trial of Feraccru vs. IV iron is not needed for regulatory purposes. Being able to demonstrate non-inferiority to IV iron is a major plus factor in terms of the product's appeal and marketability to clinicians, as can be seen from the results of the GfK online survey, where uptake is higher if non-inferiority is proven. In this case, uptake may be lower than if the only data available was that showing superiority vs. placebo.

However, the risks associated with running such a trial include the possible outcomes if non-inferiority for Feraccru is not proved. Although in mitigation the trial design would not be difficult to replicate and is very robust in design.

If the only data available is the Phase III trial data of Feraccru vs. placebo, then historical data can be used to make an indirect comparison between Feraccru, and both oral and IV comparators.

For example, an indirect comparison of Feraccru versus ferrous irons shows that Feraccru raises Hb levels by at least an equivalent amount in the first 20 weeks of therapy compared to ferrous irons when both are used at recognised therapeutic doses and Feraccru unsurprisingly demonstrates a higher incidence of GI AEs versus placebo, but the risk of these AEs is higher for ferrous irons versus placebo or IV iron than it is for Feraccru. This indirect comparison also suggests that if Feraccru was dosed at the normal levels of elemental iron that ferrous irons are prescribed at, then it might be expected that discontinuation rates and treatment related AEs would be equivalent.

However Feraccru is therapeutically effective at a total daily elemental iron dose of just 60mg, whereas ferrous irons require a total daily elemental iron dose of 600mg.

Whilst previous primary research had highlighted payers concerns regarding "indication creep", the research carried out by GfK did not confirm this. On the whole, payers that GfK interviewed viewed IDA as a whole, and did not necessarily differentiate between patients' underlying conditions. They viewed Feraccru as being suitable to be used across additional indications, e.g. in womens health and oncology, with little additional evidence requirements.

Pricing and reimbursement

Current pricing[47] of iron products is shown in the following tables. Table 10 shows the monthly ex-factory price of oral iron. It is worth noting that patients can also obtain low-dose oral iron as an over-the-counter medicine, which does not need prescribing by a physician, although these are not considered effective at treating ID/IDA with a pathological cause. OFPs are inexpensive, and the price of ferrous sulphate has been used as a benchmark, as it is considered the gold standard oral treatment. It is worth noting whilst ferrous sulfate is inexpensive, the high non-adherence to oral iron therapy leads to significant treatment failures and unnecessary follow-up investigations, [48] which will lead to a higher total cost of treatment.

Also included is the cost of oral ferrous gluconate, which has been able to achieve higher prices than those of ferrous sulfate.

Table 10: Monthly cost of oral ferrous sulphate treatment

Product	Germany	Spain	UK	France	Italy	US
Ferrous sulphate	£4.08 to £6.50 €5.80 to €9.24	N/A	£2.10 to £3.46	N/A	£1.42 €2.02	£0.76 to £1.15 $1.20 to $1.80
Modified-release ferrous sulphate	£3.51 €4.98	£1.41 to £1.48 €2.00 to €2.10	£2.26 to £6.92	£0.84 €1.20	£1.58 to £1.60 €2.25 to €2.27	£1.53 to £12.67 $2.40 to $18.00
Ferrous gluconate	£3.77 to £11.31 €5.36 to €16.07	£4.66 to £14.21 €6.63 to €20.19	£7.32 to £10.99	N/A	£3.52 to £10.58 €5.01 to €15.03	£0.84 to £2.61 $1.32 to $4.09

Prices are given at the calculated ex-factory price (Europe) and Wholesale Acquisition Cost (WAC) in the US.

Price ranges occur because of different dosing recommendations, e.g. 2 to 3 tablets per day, and because of the availability of multiple brands.

Exchange rates of 1 EUR: 0.704 GBP and 1 USD: 0.637 GBP used

[47] All prices were taken from the following sources: BNF online January 2016; roteliste.de January 2016;onmeda.es, January 2016; Analy$ource.com January 2016 , codifa.it January 2016

[48] Tolkien Z et al. (2015) Ferrous Sulphate Supplementation Causes Significant Gastrointestinal Side-Effects in Adults: Asystematic Review and Meta-Analysis. PLoSONE10(2):e0117383

Pricing of IV iron preparations is included in Table 11. The purpose of this table is to give an indication of the ex-factory price of IV iron preparations per gram of iron delivered (note that patients may need approximately 2g to 4g per year depending on their condition). Actual dosing of IV iron preparation depends on a number of factors, including patient body weight and Hb level whilst the total amount required per patient per year will depend on a number of factors including severity of their underlying disease causing IDA to re-occur, frequency of visits to specialist and testing for IDA.

Table 11: Price of IV iron per gram of iron delivered

Name	Brand	Germany	Spain	UK	France	Italy	USA
Ferric carboxy-maltose	Ferinject [EU]/ Injectafer [US]	£197.58 €280.65	£139.19 €197.72	£134.95	£140.80 €200.00	£115.64 €164.26	£738.07 $1158.67
Iron sucrose	Venofer	£115.09 €163.48	£58.07 €82.48	£76.16	Price N/A	£159.20 €226.14	£305.76 $480.00
	Fermed	£86.51 €122.88	N/A	N/A	N/A	N/A	N/A
	FerIV / Hierro Sacarosa	N/A	£58.07 €82.48	N/A	N/A	N/A	N/A
Iron dextran	Cosmofer [EU]/ INFeD [US]	N/A	N/A	£69.74	N/A	N/A	£169.38 $240.60
	Dexferrum	N/A	N/A	N/A	N/A	N/A	£229.32 $360.00
Ferric gluconate	Ferrlecit	£50.89 €72.29	N/A	N/A	N/A	N/A	£324.11 $508.80
Ferumoxytol	Feraheme	N/A	N/A	N/A	N/A	N/A	£802.32 $1259.53

Exchange rates of 1 EUR: 0.704 GBP and 1 USD: 0.637 GBP used

Based on the available pricing information, the theoretical annual drug cost can be calculated, as shown in Table 12.This excludes the costs of administration which can be significant but for which benchmark data is not available.

Table 12: Calculated annual cost of IDA in IBD and CKD (drug-acquisition cost only)

Name	Brand	Indication	Germany	Spain	UK	France	Italy	USA
Ferric carboxy-maltose	Ferinject [EU]/ Injectafer [US]	IBD	£395.16	£278.39	£269.90	£281.60	£231.28	£1476.14
		CKD	£790.31	£556.78	£539.80	£563.20	£462.56	£2952.28
		Average across indications	£592.74	£417.59	£404.85	£422.40	£346.92	£2214.21
Iron sucrose	Venofer	IBD	£230.19	£116.13	£152.32	N/A	£318.41	£611.52

		CKD	£460.39	£232.26	£304.64	N/A	£636.81	£1223.04
		Average across indications	£345.29	£174.20	£228.48	N/A	£477.61	£917.28
	Fermed	IBD	£173.02	N/A	N/A	N/A	N/A	N/A
		CKD	£346.03	N/A	N/A	N/A	N/A	N/A
		Average across indications	£259.53	N/A	N/A	N/A	N/A	N/A
	FerIV / Hierro Sacarosa	IBD	N/A	£116.12	N/A	N/A	N/A	N/A
		CKD	N/A	£232.25	N/A	N/A	N/A	N/A
		Average across indications	N/A	£174.18	N/A	N/A	N/A	N/A
Iron dextran	Cosmofer [EU]/ INFeD [US]	IBD	N/A	N/A	£139.48	N/A	N/A	£306.52
		CKD	N/A	N/A	£278.96	N/A	N/A	£613.05
		Average across indications	N/A	N/A	£209.22	N/A	N/A	£459.78
	Dexferrum	IBD	N/A	N/A	N/A	N/A	N/A	£458.64
		CKD	N/A	N/A	N/A	N/A	N/A	£917.28
		Average across indications	N/A	N/A	N/A	N/A	N/A	£687.96
Ferric gluconate	Ferrlecit	IBD	£101.78	N/A	N/A	N/A	N/A	£648.21
		CKD	£203.57	N/A	N/A	N/A	N/A	£1296.42
		Average across indications	£152.67	N/A	N/A	N/A	N/A	£972.32
Ferumoxytol	Feraheme	IBD	N/A	N/A	N/A	N/A	N/A	£1604.64
		CKD	N/A	N/A	N/A	N/A	N/A	£3209.28
		Average across indications	N/A	N/A	N/A	N/A	N/A	£2406.96

Assumptions: patients receive 2g (for IBD) or 4g (for CKD) IV iron per year.

Exchange rates of 1 EUR: 0.704 GBP and 1 USD: 0.637 GBP used

In addition to the drug cost for IV iron, there are additional costs associated with administration. These include nurse time and other associated costs of administration. Whilst these costs are recognised in the different markets, their importance varies between markets, and between different indication states, and patient sub-groups. As no publically referenced data has been identified for administration costs, these have not been included in Table 11.

GfK asked interviewees for their unprompted view on the pricing of Feraccru, before testing some specific price points).

Table 13: Unprompted price expectations for Feraccru per month

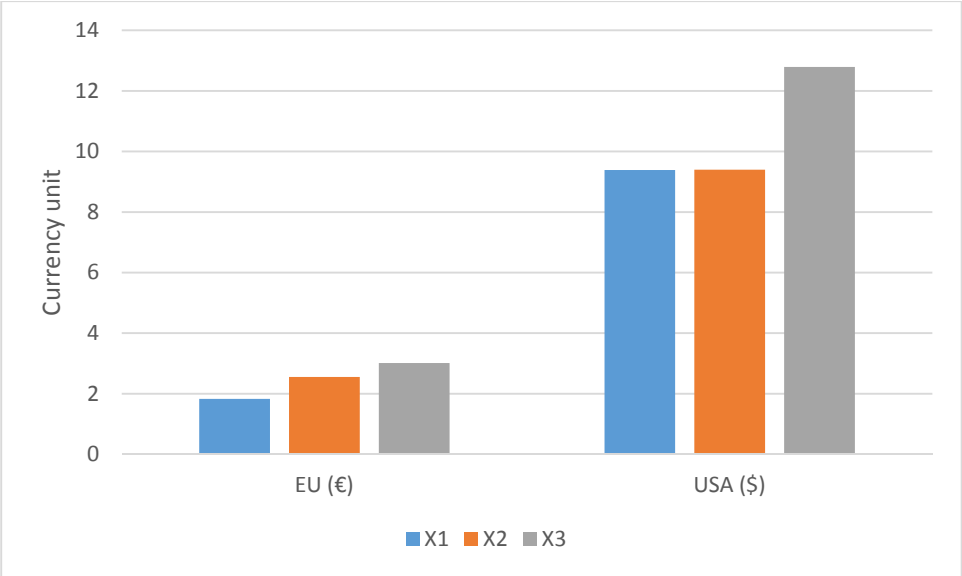
Feraccru profile	Germany (€)	Spain (€)	UK (£)	US ($)
Superior to placebo (X1)	*90*	*120, 120*	*75*	*300, 300, 300, 300, 480*
Non-inferior to IV iron (X2)	*30, 60, 120*	*132, 132, 132*	*45, 50, 75*	*300, 300, 300, 300, 480*
Superior to IV iron (X3)	*60, 120, 120*	*132, 144, 144*	*45, 75, 180*	*300, 480, 480, 500, 530*

Note that these price expectations are based on a very small sample size, and should be seen only as indicative of the price trends that might be expected if Feraccru succeeds in showing non-inferiority to IV iron.

The pricing of Feraccru with data showing it is superior to placebo was mixed amongst payers; some payers believed that the relevant pricing comparator was OFPs, hence the split in price expectations.

When calculated at a daily price expectation for the EU and US, as shown in Figure 15, it can be seen that price expectations are close to that of actual target net average price in the EU (for X1 and X2), and are significantly higher in the US. When the proposed price was shared with respondents, the majority believed that it was a very reasonable price, particularly considering the costs that would be saved through not having to administer IV iron.

Figure 15: Mean daily price expectation for Feraccru



Source: based on responses from in-depth interviews with payers

Likelihood of reimbursement/acceptance on formulary

GfK asked payers the likelihood of Feraccru gaining reimbursement and/or formulary approval in their markets, and any additional data requirements that would be needed. Payers' opinions varied as to what the most likely pricing comparator would be. Some considered that OFPs would be the most likely comparator. However, given the Phase III trial population (i.e. patients who had failed on OFPs, or who are unsuitable for OFPs), GfK believes that IV iron represents a more appropriate clinical and pricing comparator.

Overall the X2/X3 TPPs received more favourable reimbursement/formulary acceptance than did X1 (supriority vs placebo) which was considered a minimum expectation for a new agent. (However, given the relatively small sample of payers interviewed GfK would recommend additional research to study further). All payer interviewed also felt that the Ferarrcu TPPs would be made available for formulary assessement within the year.

"They look to have done all they need to do - placebo and head to head trials, which is what they would want to see. It is priced reasonably. Wouldn't generate much discussion at P&T committee meetings" US Regional Payer

Risk factors

- The level of unmet need associated with IDA therapy is moderate, and respondents exhibited low awareness of the need for new therapies. This will require Shield Therapeutics to invest in education and awareness campaigns to generate a 'call to action' amongst key customers
- Demonstration of non-inferiority of Feraccru vs IV iron in the Phase IIIb will position Feraccru away from oral ferrous products (OFPs) and towards premium pricing
    - Furthermore, GfK's research suggests that Feraccru's pricing potential is greater than Shield Therapeutics commercial expectation, especially if Phase IIIb trials are positive and demonstrate non-inferiority vs. IV iron
- Larger, more established competitors (e.g. Galenica) will continue to promote IV iron products against oral iron products through clinical trial and promotional activity, requiring investment from Shield Therapeutics to counter and manage this threat
- Market expansion opportunity into CHF, Women's Health, Patient Blood Management and Paediatrics appear viable and acceptable amongst payers interviewed by GfK (GfK recommends further research amongst payers to fully validate this aspect)
- Lead in strategy for Feraccru is to switch patients from IV iron but may be challenged by the fact that:
    - The cost effectiveness vs. IV iron argument is acceptable to payers but GfK research with payers also indicated that a significant proportion of payers are less

aware of non-drug costs associated with IV iron and awareness and education is required

- Oral therapy option for CKD5 patients less relevant as they are already undergoing dialysis in hospital and can be simultaneously given IV iron
- Adherence issues with oral therapies will be hard to overcome vs. IV iron especially in CKD market where patients already have a high pill burden

- Likelihood for reimbursement/formulary approval is higher in scenario X2 (non-inferiority to IV iron TPP) as compared to scenario X1 (superiority to placebo) which further reinforces the need for positive phase IIIb data
- For the IDA market in IBD patients, there may be a need to reach out to primary care physicians (PCPs/GPs) and office based clinicians (in Germany) to ensure that Feraccru's value is properly understood, and avoid the risk of community-based physicians switching to cheaper OFPs. Utilisation of KOL/Specialist peer driven education and awareness campaign will look address this aspect
- Market expansion can be driven by reaching out to patients/patient groups to encourage a 'push' strategy, especially in the US for IBD and other expanded indications (Women's Health)

PT20

Epidemiology

Number of patients

Decision Resources Group Inc ("Decision Resources"), a biopharmaceutical analysis and data provider, has calculated the dialysis-dependent population for the US and Europe. It estimated that in the US, in 2012 there were 446,400 dialysis patients. In Europe this figure was 212,200. By 2017, Decision Resources estimated that these numbers would have risen to 495,800 in the US and 221,700 in Europe.[49]

Data on CKD are scarce, with data coming from medical databases and population surveys, with CKD data from medical databases tending to overestimate the prevalence of diseases.[50]

The prevalence of stage 3–5 CKD in population-based studies ranges from 3.6% (Norway) to 7.2% (Germany) in males and from 6.2% (Italy) to 10.2% (Iceland) in females. The prevalence of stage 3–5 CKD appears reasonably similar across EU countries,[51] and in these calculations, GfK has assumed a prevalence of 6% for CKD Stage 3 and 0.5% for CKD Stage 4, for the adult population. This gives a total patient population of approximately 15.5 million patients in the US and 16.5 million in the EU5, who have CKD stages 3 to 5.

[49] DecisionBase 2014. Hyperphosphataemia. Payer and Physician Receptivity to Novel Treatments – Which Emerging Drugs Excite Them? April 2014
[50] Zoccali C, Kramer A, Jager KJ. Chronic kidney disease and end-stage renal disease. NDT Plus (2010_ 3: 213-224
[51] Zoccali C, Kramer A, Jager KJ. Chronic kidney disease and end-stage renal disease. NDT Plus (2010_ 3: 213-224

Number of patients undergoing pharmaceutical treatments

Decision Resources again calculated the number of dialysis patients who are treated with phosphate binders, based on their own primary research. A number of surveys were also conducted among nephrologists and audits were carried out of patient-level data from dialysis patient records to determine phosphate binder treatment rates of patients undergoing dialysis, from which it was estimated that 74% of dialysis patients in Europe are treated with phosphate binders.[52] A later study from Infusion Pharma Consulting suggested that approximately 80% of dialysis patients in the US are treated with phosphate binders.[53] This would indicate that approximately 377,000 dialysis patients in the US and 160,500 dialysis patients in the EU5 are being treated with phosphate binders.

Table 15: Estimates of CKD patients who are treated for Hyperphosphataemia

Parameter	CKD Stage 3	CKD Stage 4 (non-dialysis)	CKD Stage 5 (dialysis)
United States			
Number of patients	15 million	1,268,000	471,100[54]
% receiving phosphate binders			80% (377,000)
Europe (EU5)			
Number of patients	16.1 million	1,342,600	216,950[55]
Number of patients receiving phosphate binders			161,000 (74%)

Percentages may not add up due to rounding

Adult population (age > 15yrs) estimates are taken from Eurostat for EU5 and United States Census Bureau

Non-dialysis patients are much less likely to receive phosphate binders for treatment of hyperphosphataemia, but there was no consensus amongst interviewees as to when to begin treatment. Of the approved phosphate binders, there are only a few which are approved for use in pre-dialysis patients (these include Fosrenol (lanthanum carbonate) and Phosex (calcium acetate). Fexeric (ferric citrate) was approved by the EMA in July 2015 for hyperphosphataemia in adults with CKD (i.e. pre-dialysis or dialysis). In the US, it is only approved for patients on dialysis.

Current unmet needs

Dialysis patients are routinely treated with a phosphate binder, but there is a high pill burden and high rates of adverse events with current therapies. This leads to poor adherence and reduced therapeutic benefit.

[52] DecisionBase 2014. Hyperphosphataemia. Payer and Physician Receptivity to Novel Treatments – Which Emerging Drugs Excite Them? April 2014
[53] Infusion Pharma Consulting. PT20 Commercial Assessment – Final Report. May 2015
[54] Based on estimates from Decision Resources 2014, with data sourced from US and EU renal registries
[55] Based on estimates from Decision Resources 2014, with data sourced from US and EU renal registries

A survey carried out in 2014 amongst 60 US and 30 European nephrologists by Decision Resources, asked respondents to consider the efficacy, safety and tolerability, and delivery of currently available treatments for hyperphosphataemia and indicate the level of unmet needs for a set of key hyperphosphataemia clinical attributes.

The five unmet needs with the highest unmet need score identified were:

- A greater effect on improving mortality
- Lower pill burden/fewer pills per day
- Greater effect on reducing serum phosphate levels
- Reducing dose frequency
- Lower risk of vascular calcification

Therapy market

Market overview

Treatment for hyperphosphataemia generally includes the use of phosphate binders in late-stage CKD and dialysis patients. Dialysis patients are far more likely than pre-dialysis patients to be prescribed a phosphate binder, and are used in the majority of dialysis patients to control phosphate levels by preventing the absorption of phosphate. They have evolved over multiple generations, with multiple classes being available (calcium-based and non-calcium based); iron–based binders are the newest class, with two products available in the US and EU (Velphoro and Auryxia/Fexeric).

Due to ease of reimbursement, US nephrologists prefer sevelamer-based binders as their first-line binder to treat dialysis patients diagnosed with hyperphosphataemia, although a step therapy approach starting with calcium-based binders and then switching to non-calcium binders may have to be taken.[56] The majority of binder-treated patients in the US are only on one phosphate binder, most often a sevelamer-based binder.

In Europe, patients with hyperphosphataemia are most likely to be prescribed a small dose of calcium-based binders. Where these drugs are contra-indicated, sevelamer or lanthanum carbonate are used.[57]

[56] DecisionBase 2014. Hyperphosphataemia. Payer and Physician Receptivity to Novel Treatments – Which Emerging Drugs Excite Them? April 2014
[57] DecisionBase 2014. Hyperphosphataemia. Payer and Physician Receptivity to Novel Treatments – Which Emerging Drugs Excite Them? April 2014

Table 16: Type and features of phosphate binders available in the US and Europe

Class	Brand (generic)	Daily pill burden	Efficacy/safety information
Calcium	Calcium carbonate		
	Calcium acetate (Phoslo)	9 to 12	
Resin	Renagel/Renvela (sevelamer hydroxide/sevelamer carbonate)	8 to 9	In clinical trials, sevelamer has been shown to be effective in reducing serum phosphorus in patients receiving haemodialysis or peritoneal dialysis[58]
Heavy metal	Fosrenol (lanthanum carbonate)	3	A total of 1130 patients with chronic renal failure treated with maintenance haemodialysis or CAPD were studied in two phase II and two phase III studies. Three studies were placebo controlled (1 fixed dose and 2 titrated dose designs) and one included calcium carbonate as an active comparator[59]
Iron	Velphoro (sucroferric oxyhydroxide) (US only)	3	Phase III study vs. sevelamer demonstrated that 5–12.5 g/d significantly reduces serum phosphorus in haemodialysis patients. The 5 g/d and 7.5 g/d dosages showed similar efficacy to 4.8 g/d of sevelamer-HCl. The adverse events rate was similar for Velphoro and sevelamer-HCl.[60] Phase III study vs. sevelamer carbonate in dialysis patients, which demonstrated Velphoro was effective in lowering serum phosphorus, with similar efficacy to sevelamer carbonate, a lower pill burden, and better adherence[61]
	Auryxia (US)/ Fexeric (EU) (ferric citrate)	Average 8 to 9	Phase III study in haemodialysis patients with hyperphosphataemia demonstrated efficacy as a phosphate binder in a dose-dependent manner.[62] Phase III study vs. sevelamer hydrochloride demostrated non-inferiority[63]

[58] Renagel Summary of Product Characteristics
[59] Fosrenol Summary of Product Characteristics
[60] Wüthrich RP, Chonchol M, Covic A, et al. Randomized clinical trial of the iron-based phosphate binder PA21 in hemodialysis patients. Clin J Am Soc Nephrol 2013; 8: 280–289
[61] Floege J, Covic AC, Ketteler M, et al. A phase III study of the efficacy and safety of a novel iron-based phosphate binder in dialysis patients. Kidney Int 2014; 86: 638–647
[62] Dwyer JP, Sika M, Schulman G, et al. Collaborative Study Group. Dose-response and efficacy of ferric citrate to treat hyperphosphatemia in hemodialysis patients: a short-term randomized trial. Am J Kidney Dis 2013; 61: 759–766
[63] Yokoyama K, Akiba T, Fukagawa M, et al. A randomized trial of JTT-751 versus sevelamer hydrochloride in patients on hemodialysis. Nephrol Dial Transplant 2014; 29: 1053–1060

The choice of phosphate binder depends on a number of factors:[64]

- Whether or not it contains calcium (guidelines recommend restricting the dose of calcium-based phosphate binders in the presence of persistent or recurrent hypercalcemia)
- The potential for gastintestinal (GI) absorption of the active moieties that could be harmful or beneficial to the body, e.g. magnesium (absorbed from magnesium-carbonate-containing phosphate binders) could act as an anti-arrythmic and could have inhibitory actions on vascular calcification.
- Whether the phosphate binders can bind not only phosphate, but also harmful or useful substances in the gut, e.g. sevelamer binds several compounds in the gut apart from phosphate, such as cholesterol, urate and uremic toxins.
- Adherence to phosphate binder therapy, with phosphate binders accounting for approximately one-half of the daily pill burden in haemodialysis patients, this can lead to non-adherence.
- Effect on FGF23 serum levels. Several prospective studies[65] [66] [67] [68] in populations of pre-dialysis CKD, incident and prevalent ESRD on haemodialysis and kidney transplant recipients demonstrate that elevated circulating FGF23 levels are independently associated with an increased risk of cardiovascular events and mortality. The effect of different phosphate binders on circulating FGF23 levels could have important implications on morbidity and mortality in CKD patients. Non-calcium-based phosphate binders have been shown to decrease FGF23 while calcium-based phosphate binders have not. A recent study showed that there was a negative relationship between iron administration and serum intact FGF23 level in a dialysis population, in contrast to what is seen for the general population. Therefore, if high levels of FGF23 are harmful, iron therapy may have a beneficial effect on cardiovascular events and mortality in dialysis patients by reducing FGF23 levels.[69]

Guidelines

Most patients experiencing hyperphosphataemia are initially advised by clinicians to manage their condition through diet modification with reduced phosphate intake. However, this is rarely sufficient to control serum phosphate levels, and pharmaceutical intervention is required in the majority of patients. The standard treatment for patients with persistent hyperphosphataemia is a phosphate binder delivered orally and taken with food as the primary aim of the binder is to bind phosphate in the food, thereby preventing it from being absorbed.

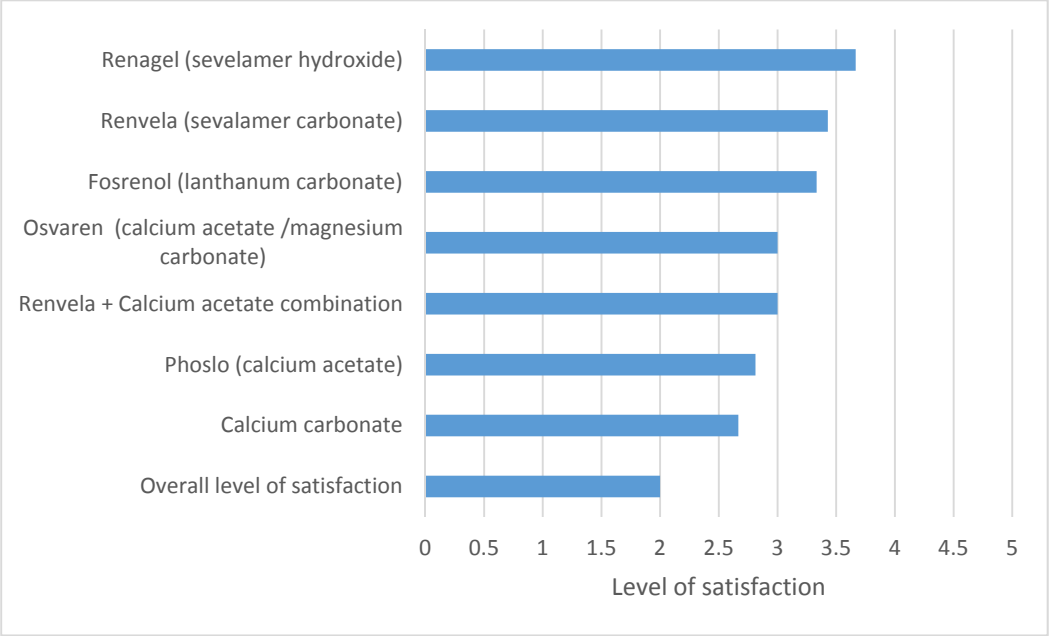
[64] Negri AL, Torres PAU. Iron-based phosphate binders: do they offer advantages over currently available phosphate binders? Clin Kidney J. 2015 Apr; 8(2): 161–167.
[65] Kendrick J, Cheung AK, Kaufman JS, et al. HOST Investigators. FGF-23 Associates with death, cardiovascular events, and initiation of chronic dialysis. J Am Soc Nephrol 2011; 22: 1913–1922
[66] Gutierrez OM, Mannstadt M, Isakova T, et al. Fibroblast growth factor 23 and mortality among patients undergoing hemodialysis. N Engl J Med 2008; 359: 584–592
[67] Jean G, Terrat JC, Vanel T, et al. High levels of serum fibroblast growth factor (FGF)-23 are associated with increased mortality in long haemodialysis patients. Nephrol Dial Transplant 2009; 24: 2792–2796
[68] Wolf M, Molnar MZ, Amaral AP, et al. Elevated fibroblast growth factor 23 is a risk factor for kidney transplant loss and mortality. J Am Soc Nephrol 2011; 22: 956–966
[69] Deger SM, Erten Y, Pasaoglu OT, et al. The effects of iron on FGF23-mediated Ca-P metabolism in CKD patients. Clin Exp Nephrol 2013; 17: 416–423

Kidney Disease Improving Global Outcomes (KDIGO) guidelines recommend that stage 3-5 CKD-ND and dialysis patients receive phosphate binders for the treatment of hyperphosphataemia, which is defined in these guidelines as > 4.6 mg/dL for both CKD-ND and dialysis patients. The Kidney Disease Outcomes Quality Initiative (KDOQI) guidelines identify the normal range for stage 3 and stage 4 CKD-ND patients as 2.7-4.6 mg/dL and 3.5-5.5 mg/dL for dialysis patients. In general, physicians in Europe follow the KDIGO guidelines and physicians in the US follow the KDOQI guidelines. Both sets of guidelines recommend restricting the dose of calcium-based phosphate binders in the presence of persistent or recurrent hypercalcemia.

Perception of therapy options

Current therapies for the treatment of hyperphosphataemia are less than satisfactory. GfK surveyed a small group of nephrologists about their level of satisfaction with current treatments, where a score of 1 indicated a lack of satisfaction, and a score of 5 indicated that they were fully satisfied with a particular therapy. The newer therapies (sevelamer and lanthanum) have higher levels of satisfaction, as they do not have the potential issues with causing hypercalcification that the calcium based binders have.

Figure 16: Nephrologists' level of satisfaction with current phosphate binder treatments (US&EU)



"Calcium based binders are controversial in terms of calcification. Should we be ditching them? Non-calcium based ones have bad tolerability, 40-50% of patients struggle either in terms of tolerability per se or pill burden. Adherence will be bad because of both the side-effects and the burden." UK KOL, Nephrologist

There is a clear need for a treatment which can offer good efficacy in reducing phosphate levels, with few side effects and a low pill burden.

PT20 and its place in the market

Description

PT20 is a novel iron-based phosphate binder for the treatment of hyperphosphataemia related to dialysis or non-dialysis dependent chronic kidney disease (CKD).

PT20 is currently available (based on the Phase 2b drug product) as an 800mg oral tablet, including 200mg ferric iron.

Competitive position

PEACH study

The PEACH Phase II study was conducted in the US in approximately 20 dialysis centres. It was a randomised study of PT20 compared to placebo, in reducing blood phosphate in subjects receiving haemodialysis (ESRD). It enrolled 153 randomised subjects who received one of four dose levels of PT20 (400mg to 3200mg per dose) or placebo.

Patients were initially screened against inclusion criteria for the study. Patients had to be dialysis dependent, taking a phosphate binder, with phosphate levels of 4-8mg/dL and ferritin <1000ng/mL. If eligible patients then underwent a wash-out period of 28 days, after which time they were randomised to one of the four PT20 treatment groups, or to placebo. After 28 days treatment with either PT20 or placebo, there was then a 14 day follow-up period.

The study was conducted successfully with few discontinuations or major protocol violations. The primary efficacy endpoint, i.e. the change in serum phosphate level from Baseline (Visit 7, Day 1) to Visit 11 (Day 29), was met ($p<0.001$) and all population and sensitivity analyses were also statistically significant.

A clear dose response was achieved in this fixed dose study. All dose groups had a mean phosphate reduction greater than the Placebo group, with the mean reduction in phosphate increasing from the lowest dose group to the highest dose group.

There were very few discontinuations due to adverse events. Most AEs were GI in nature (diarrhoea, flatulence, discoloured faeces, abdominal pain/discomfort, nausea, vomiting) and did not appear to be dose related in this study (with possibly vomiting in the highest dose group). There was no pattern of serious AEs attributable to study medication. Although the period of no concomitant iron medication was short (just 2 weeks), there was a 32ng/mL rise in Ferritin in PTC20 treated subjects compared to a 53ng/mL fall in the Placebo group.

Adherence with medication was 79% in the placebo group and 61% to 76% in treatment groups; there was no pattern of worsening adherence with dose/tablet number.

Data from the phase IIb study suggests there is a possibility of reducing pill count and this will be further exploited by increasing the API load in the tablets used in future studies.

Competitive position vs. Auryxia/Fexeric (ferric citrate) and Velphoro(sucroferric oxyhyroxide)

Clinical trials suggest that both ferric citrate and sucroferric oxyhydroxide are effective phosphate binders, non-inferior to currently used phosphate binders. Ferric citrate may be more suited for the

treatment of chronic hyperphosphatemia in CKD patients requiring iron supplements but its use may be hampered by unwanted concomitant aluminium absorption. Sucroferric oxyhydroxide may be more suited for hyperphosphatemic CKD patients not requiring iron supplementation and its major benefit would be a low pill burden – although the tablets are large and require chewing rather than swallowing which may pose compliance issues.

Based on the responses of the nephrologists and payers who commented on target product profile, they believed that whilst a product with a dual-purpose (i.e. ability to supplement iron as well as act as a phosphate binder) was useful, they did not see a particular competitive advantage over currently available products. Having said this, of the nephrologists interviewed, the majority said they would prescribe PT20 to at least some new patients, or would switch patients from one therapy to this one.

There are relatively few late stage products in development for hyperphosphataemia:

Fermagate (Alpharen™) is a proprietary phosphate binder being developed by OPKO Health for the treatment of hyperphosphataemia in patients undergoing haemodialysis. According to OPKO, Phase III development is in progress in the US and in Europe. Previously, two phase III trials of fermagate were initiated by Ineos Healthcare, but were subsequently terminated. The trials were to assess the efficacy of fermagate in patients with chronic kidney failure who needed haemodialysis, compared with sevelamer hydrochloride (NCT00844662), or lanthanum carbonate (NCT00841126). According to OPKO Health's website, further Phase III development is planned to start in 1H'16.[70]

Tenapanor is being developed by Ardelyx for the oral treatment of hyperphosphataemia. Tenapanor is a small-molecule, selective inhibitor of NHE3 (sodium hydrogen exchanger 3), which is present on the surface of the intestinal epithelia. Phase II development for hyperphosphataemia in patients with end-stage renal disease is underway in the US, the UK, Slovakia and Poland.

In a randomised, double-blind, placebo-controlled phase IIb trial that evaluated the safety and tolerability of tenapanor film-coated tablet and its effects on serum phosphorus in patients with end-stage renal disease who are on haemodialysis for the treatment of hyperphosphataemia, the primary endpoint was met. (NCT02081534; EudraCT2013-004319-33; D5613C00001). The study was completed in November 2014, and enrolled patients in the US, the UK, Poland and Slovakia. Ardelyx plans to commence a phase IIb trial to assess the optimal dosing regimen for tenapanor for the treatment of hyperphosphataemia in dialysis patients. The trial is expected to commence by December 2015, with results expected in the second half of 2016.[71]

Development status and plans for PT20

Phosphate Therapeutics has carried out a pivotal Phase IIb study (PEACH), a randomised study carried out in approximately 20 US dialysis centres, investigating 4 dose levels of PT20 and placebo. This demonstrated safety and efficacy of PT20 as a phosphate binder.

[70] OPKO Health Renal website. http://www.opkorenal.com/pipeline/product_candidates.html Accessed August 3rd 2015

[71] Ardelyx press release. July 14, 2015. Ardelyx to provide updates on Research and Development Programs at today's Inaugural R&D Day in New York City. http://ir.ardelyx.com/releasedetail.cfm?ReleaseID=921886 Accessed August 3rd 2015

Subject to regulatory agency guidance and agreement currently anticipated plans for phase III clinical plans involve carrying out a Phase III non-inferiority study, most likely vs. sevelamer (as this is the market leader). The Phase III study will be used to optimise and differentiate PT20's label, which will investigate the co-primary endpoints of serum phosphate and ferritin score (as a measure of iron status).

The Phase 3 study design will be influenced by the End of Phase 2 discussions with the FDA planned late 2015 but it is currently envisaged that the study will enrol >500 subjects, and is planned to include a placebo-controlled arm for at least part of the study. The study will probably be multi-national, with the data used for US and EU submissions (along with the existing Phase II data).

For Japan and Asia, further studies would include as Phase II and pharmacokinetic study in dialysis subjects, a local Phase 3 study in dialysis subjects, and Phase II and Phase 3 studies in patients with CKD. Development would be likely via a third party partner in these territories.

There are a number of development options for PT20:

- Dosing – development of dose form and tablet alternatives. Look at BD dosing for patients who have 2 main meals, and conversion dose from sevelamer
- Target population – look at "refractory" or hard to treat population (e.g. those patients who are currently taking 2 phosphate binders). In pre-dialysis CKD patients, perform a study based on cardiovascular mortality, looking at CKD progression with iron-based binders (i.e. Keyrx/Aurxia cost/risk share)
- Iron absorption – incorporate a co-primary endpoint into the Phase III study to include IV iron and ESA use. HIF p-h-I factor combined use in HD subjects, also a phase II study of iron absorption in CKD.

Regulatory status and plans

The strategy for PT20 is to be confirmed and fine-tuned following further dialogue with key regulatory bodies.

In the US, a pre-IND meeting has been held with the FDA (in April 2013), in which data to support the Phase IIb study, the Phase IIb study design and overall development plan were discussed. The IND to conduct clinical trials with PT20 was approved in April 2014. The company plans to conduct an end of phase 2 meeting with FDA before the end of 2015.

In Europe, a Scientific Advice meeting is planned for late 2015, at which the development plan, including the Phase 3 trial design will be discussed.

In terms of the non-clinical data, the current FDA required programme is largely complete and will be discussed at the next meeting with the agency:

- 14 and 28 day rat studies completed
- 26 week rat study to support Phase III completed
- *In vitro* drug-drug interaction studies planned for 2015
- Reproductive and carcinogenicity studies may be required for EU approval

The clinical studies undertaken/planned are as follows:

- Multiple dose placebo controlled phase IIb (include PK substudy) – completed
- Phase 3 programme design to be agreed with Agencies

Paediatric studies will be required, with Paediatric Investigation Plan submission expected in 2016.

Manufacturing status and plans

The PT20 drug substance process has been developed from the laboratory (0.5g) to cGMP 20kg scale. The requirements for the 28 day and 6 month preclinical and Phase I and IIb requirements have been met. Twelve months real time stability and 6 months accelerated data (no change) have been obtained, and the analytical methods have been developed and validated.

400mg and 800mg drug product tablets were developed for Phase IIb study, with 9 months real time stability and 6 months accelerated data obtained.

Phase III drug substance and drug product planning has been carried out. Drug substance and drug product manufacturing is being carried out during the remainder of 2015 and early 2016. Drug substance and drug product stability studies will be conducted following manufacture to support the eventually agreed phase 3 programme.

Market potential

The annual US market for phosphate binders is >$1bn in the US and is approaching $2bn globally.[72]

With concern over the long term safety of calcium binder use the use of calcium-based binders is likely to decline over time.

Based on the responses from nephrologists, a novel iron-based phosphate binder, such as PT20, should be able to take a small share of the binder market, if sold at a premium price. Shield will likely already have a sales force active in targeting nephrologists (for promotion of Feraccru) and PT20 will add another product to the portfolio.

One option would be to target PT20 at patients who are difficult to treat, e.g. refractory patients, which would provide potential for differentiation and a premium price. This may be considered by re-visiting the Phase 2 data and noting that the dose escalation was not associated with higher dropout rates which theoretically may suggest that PT20 is effective in treatment resistant patients.

An alternative strategy would be to market PT20 as a ‘me –too’ agent with a lower price, in order to gain market share (dependant on Phase 2 clinical trial results). This may be possible with a low cost of goods, and an efficient, established sales force.

Plans for commercialisation and achievements to date

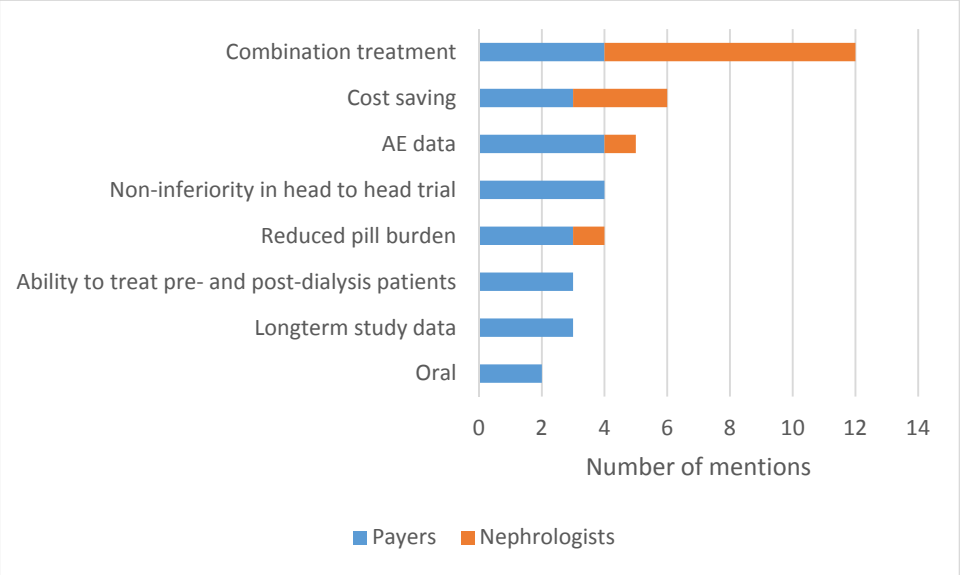
Shield Therapeutics may consider regional partnering PT20 to take it through Phase 3 development and into US, EU and Asian registration/commercialisation.

[72]Keryx corporate presentation Spring 2014

Product merits

Nephrologists and payers were asked about any advantages they could see with PT20, and their responses are captured in Figure. The key advantage was that PT20 had the potential to offer iron supplementation in addition to lowering phosphate levels, and effectively act as a combination treatment in dialysis patients. This would potentially have the impact of lowering pill burden for patients, and potentially reduce costs associated with IV iron and ESA.

Figure 17: Advantages of PT20 mentioned by Payers and Nephrologists (US&EU)



"It captures the ability to bind phosphate and give iron in one product – therefore it could be money saving. It does not contain calcium which has safety data benefits, and it may gain because of the other products already in the market will demonstrate this over time." US KOL, nephrologist

The ability to offer a treatment to both pre- and post-dialysis patients was also seen as important by payers:

"It can be attractive when thinking about formulary placement you can offer treatment for a broader patient population", US Regional Payer

Pricing and reimbursement

The purpose of Table 17 is to give an indication of the ex-factory price of phosphate binders for 28 days treatment. Prices are at the ex-factory price level (EU)/ Wholesale Acquisition Cost, WAC (US). Dose varies between patients, with prices given based on "usual dose" ranges as stated in clinical trials and dosing guidance.

Table 17: Monthly ex-factory price of phosphate binders used to treat hyperphosphataemia

Class	Generic (brand)	Germany €	Spain €	UK £	USA $
Calcium	Calcium carbonate. (Examples include Calcichew, Calcichew Forte, Adcal, CC-Nefro, Dreisacarb, Tums, Carbocal)	10.06 to 15.09	1.95 to 3.90	6.39 to 16.13	<20
	Calcium acetate. (Examples include Phoslo, Phosex, Calcium-acetat-Nephro)	16.53 to 22.04	17.68 to 23.57	10.78 to 21.17	176.85 to 235.80
	Calcium acetate/magnesium carbonate (Osvaren)	16.92 to 56.39	12.61 to 42.04	9.80 to 32.67	N/A
Resin	Sevelamer hydroxide (Renagel)	102.97 to 514.87	73.21 to 366.05	68.21 to 341.04	245.19 to 1225.93
	Sevelamer carbonate (Renvela) tabs	240.27 to 274.80	102.54 to 117.19	159.15 to 181.89	915.31 to 1046.07
Heavy metal	Lanthanum carbonate (Fosrenol) tabs	157.15 to 219.17	130.17 to 196.26	101.31 to 158.10	785.13
Iron	Sucroferric oxyhydroxide (Velphoro)	N/A	N/A	N/A	798 to 1064
	Ferric citrate (Auryxia)	N/A	N/A	N/A	943.04 to 1060.92
Colestilan	Colestilan (Bindren)	109.94 to 164.91	N/A	106.17 to 159.26	N/A

Currently the most likely pricing comparator was viewed to be sevelamer, as this is the most commonly used phosphate binder. GfK's qualitative research indicated that a 10 to 15% premium over sevelamer was viewed by payers as acceptable. However, the launch of PT20 is some way off, and the actual market pricing of phosphate binders, including impact of generic sevelamer, at this time is not clearly defined, and warrants further investigation.

Shield Therapeutics has plans that may incorporate a co-primary endpoint into the Phase III study to include IV iron and ESA use. Presently, IV iron and ESAs are part of the bundled dialysis payment in the US, while phosphate binders are paid by private insurers, Medicare part D or the patient. Any cost savings that can be demonstrated through reductions in use of IV iron, or less use of ESAs, would be cost savings for the dialysis units, while the cost of phosphate binder therapy (PT20) would be for other payers.

In the US, from January 2016, payment for oral-only renal medications (including phosphate binders) is expected to be included in the new Medicare bundled end-stage renal disease (ESRD) prospective payment system (PPS). The implementation of the ESRD PPS has generated concern within the nephrology community because of the potential for inadequate funding, with reimbursement rates for coverage of all oral-only renal medications insufficient to cover the costs, which may impact on patient quality of care.

Payers were divided on the likelihood of reimbursement for PT20 (although it was a small sample size in each market). Reimbursement/acceptance onto formulary will be dependent on price and/or

efficacy. If it is less expensive, but similar efficacy to existing products it will be reimbursed. If it is superior in efficacy to existing products, then again it will be reimbursed.

Risk factors

Based on the current clinical profile of PT20, there would appear to be little to differentiate it from other phosphate binders. If this is the case, then it is likely that price will play a key role in influencing uptake of a new product such as PT20 particularly given the forthcoming genericisation of sevelamer in the next few years.

Consideration must be given to the clinical development programme of PT20, which should be designed to enable differentiation of PT20 from the other phosphate binders. If this is not possible then PT20 can be positioned as 'me-too' agent and emphasize its dual action on phosphate and iron levels and lowering pill burden vs current therapies. In addition potential to re-visit Phase 2 data and demonstrate that dose escalation wasn't associated with high dropout rates thereby demonstrating effectiveness with hard to treat (refractory) patients (although subject to Phase 2 study outcomes).

- The main risk is the likely future genericisation of the market with the standard of care agent sevelamer leading to a price decrease in the calcium-binder class
- Consideration must be given to the clinical development programme of PT20, which should be designed to enable differentiation of PT20 from the other phosphate binders. If this is not possible then PT20 can be positioned as 'me-too' agent and emphasize its dual action on phosphate and iron levels and lowering pill burden vs current therapies.
- In addition potential to re-visit Phase 2 data and demonstrate that dose escalation wasn't associated with high dropout rates thereby demonstrating effectiveness with hard to treat (refractory) patients (although subject to Phase 2 study outcomes).

CONCLUSIONS

Overall, GfK feels that of the two key assets, Feraccru has the greatest commercial potential, firstly in the initial target patient populations, IBD and CKD pre-dialysis patients, and secondly in indications that would support market expansion, namely CHF, Women's Health and Patient Blood Management. Feraccru will be positioned for patients with inadequate clinical response to other oral agents and therefore as a clear second line therapy ahead of IV iron. Demonstration of non-inferiority vs. IV iron, through a Phase IIIb programme which meets current regulatory requirements, represents an important success factor in obtaining premium pricing.

The commercial potential for PT20 is rather more limited, based on the current target product profile, since it offers little differentiation versus current, relatively low cost treatment options in hyperphosphatemia. Nonetheless, GfK believes that PT20 represents a potential complementary revenue generating opportunity for Shield Therapeutics, which would be able to leverage the same commercial infrastructure as Feraccru and would be targeted towards the same key clinicians, particularly, nephrologists.

Situational analysis for Feraccru for IDA in IBD and/or CKD

Iron deficiency anaemia (IDA) is a severe stage of iron deficiency in which haemoglobin (or the hematocrit) declines below the lower limit of normal. IDA is defined as anaemia with biochemical evidence of iron deficiency. IDA occurs when iron stores are exhausted and the supply of iron to the bone marrow is compromised.

IDA is a common complication of inflammatory bowel diseases (IBD), with multiple causes, although iron deficiency is the most prevalent. Almost every anaemic patient with IBD demonstrates some degree of iron deficiency as a consequence of dietary restrictions, malabsorption, or intestinal bleeding. In patients with Chronic Kidney Disease (CKD), as kidney function declines and in patients with more advanced CKD stages, the incidence and prevalence of anaemia increases. IDA is also a significant consequence of other disease states including Coronary Heart Failure (CHF), Women's Health, Anaemia induced Oncology, Patient Blood Management (PBM) and Paediatric populations.

Specialists percieve that only a moderate level of unmet needs exist across both IBD and CKD patients (based on the on-line survey). Differences exist in terms of unmet needs between IBD and CKD patients. IBD patients already have existing GI issues so oral ferrous products (OFPs) are poorly tolerated but there is a perception that IV iron is an expensive alternative. There is perceived to be relatively low unmet needs for DD-CKD patients, owing to high pill burden with dialysis CKD patients and the fact that there are no major issues administering IV iron to these patients at same time as dialysis. In pre-dialysis however, where patients do not routinely present to hospital and lack of tolerance of OFPs is likely to be significant the cost and administartion associated with IV is also expected to be significant. Overall, KOLs believe that key unmets needs relate to improving the patient's quality of life, improving mode of administration and reducing medical resource utilisation (in light of drug and non-drug costs associated with IV iron administration). Payers are more concerned with efficacy and having a safe medication.

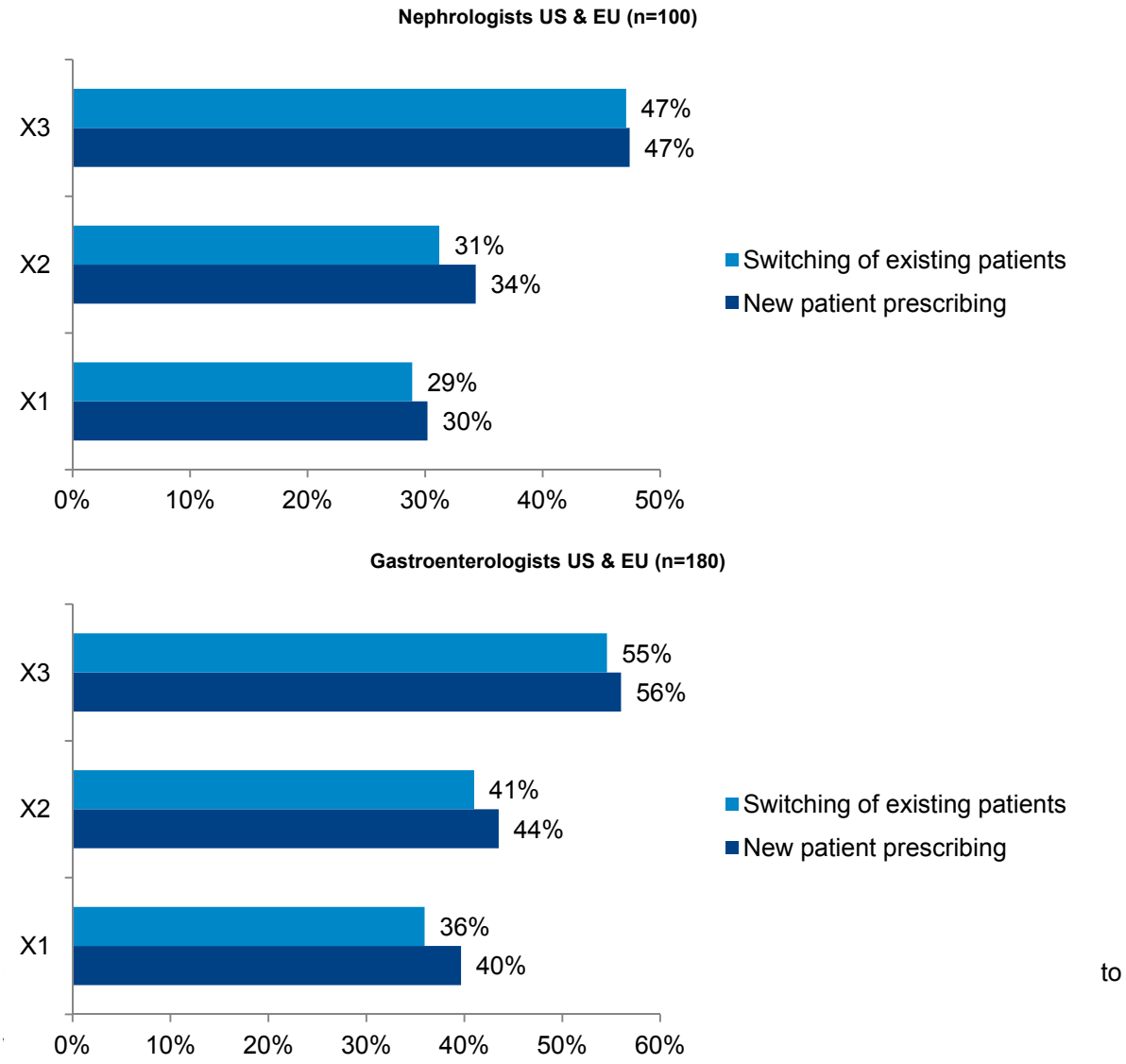
For clinical specialists, the level of satisfaction with current therapy options is moderate at best, with the IV irons (particularly Ferinject) regarded having several advantages over OFPs, such as faster and higher increase in Hb levels and replenishment of body iron stores. The only concerns mentioned in relation to IV iron related to cost of treatment associated with infusions and inconvenience for patients having to come into the hospital. This suggests that there is a need for an effective iron product, with few adverse events that is not administered through the IV route.

GfK believes that there is an opportunity for Shield Therapeutics' ST10 (novel oral ferric iron product) - Feraccru across both the IBD and CKD populations, based on the TPPs presented. (Profiles presented are in the appendix of this report).

KOLs, clinicians and payers all reacted positively to the TPPs presented for Feraccru. The majority of clinicians believed that Feraccru would offer benefits over existing treatments, namely that it is an oral treatment, which is effective, and has few adverse events associated with it.

Gastroenterologists (across US/EU) stated that they would on average consider prescribing Feraccru to between 40-56% of their new patients and between 36-55% of their switch patients (where the treating physician exchanges one medicine for another with the same therapeutic intent in patients who are already undergoing treatment), depending on the TPP achieved (X1/2/3). Nephrologists indicated that they would on average prescribe between 17-26% of their new patients and 16-26% of their switch patients to Feraccru, depending on the TPP achieved.

Figure 19: New patient prescribing of, and switching of existing patients to, Feraccru under scenarios X1, X2, and X3

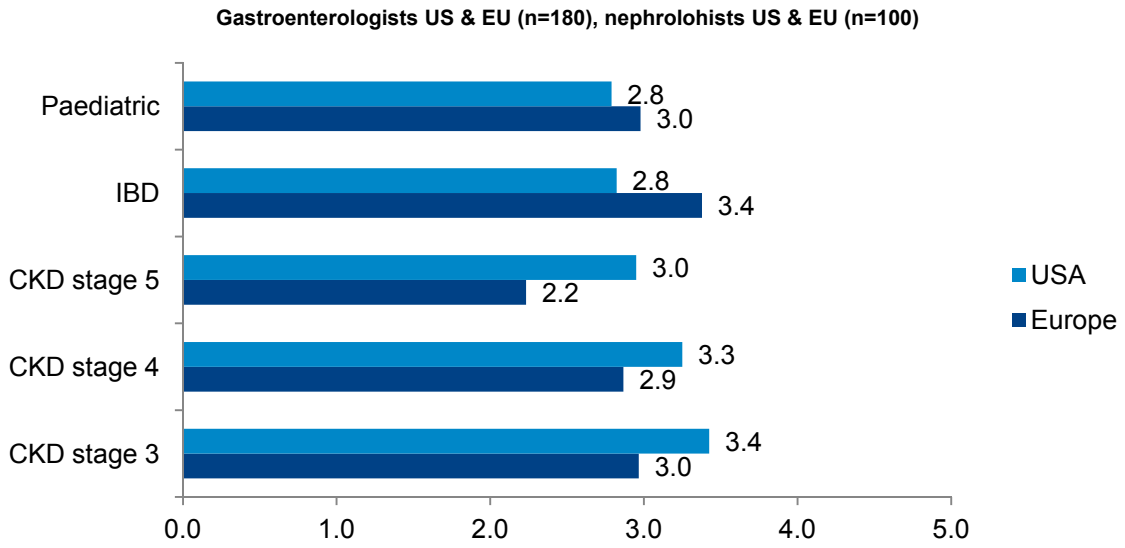


to

This was expected since IV iron was seen as an acceptable approach for CKD patients on dialysis.

On presenting the Feraccru base case profile (demonstrating superiority to placebo) to a robust sample of US/EU gastroenterologists (n=180) it was confirmed that IBD patients would be expected to benefit most from Feraccru, followed by Paediatric patients, as these patients have the greatest need for an oral treatment with a more favourable GI side effect profile. Furthermore, for the Paediatric patient population IV treatments are generally considered less appropriate. Similarly the same Feraccru profile was presented to a robust sample of US/EU nephrologists (n=100) and Feraccru was seen to offer greater clinical value in CKD stage 3 patients (pre-dialysis) than CKD 4-5 (dialysis patients), since the latter group receives regular dialysis and can be given IV iron treatment simultaneously.

Figure 20: Ability of Feraccru to meet unmet needs associated with current IDA treatments



GfK also presented nephrologists and gastroenterologists with the scenario in which Feraccru was shown to be non-inferior to IV iron (a clinical trial vs. IV iron is planned). Clinicians were then asked to score their level of interest, and again what percentage of new patients they would prescribe Feraccru, given this additional data. The mean scores for both groups increased, indicating that clinicians were more likely to prescribe Feraccru for new patients and switch more patients to Feraccru, were such data to be available.

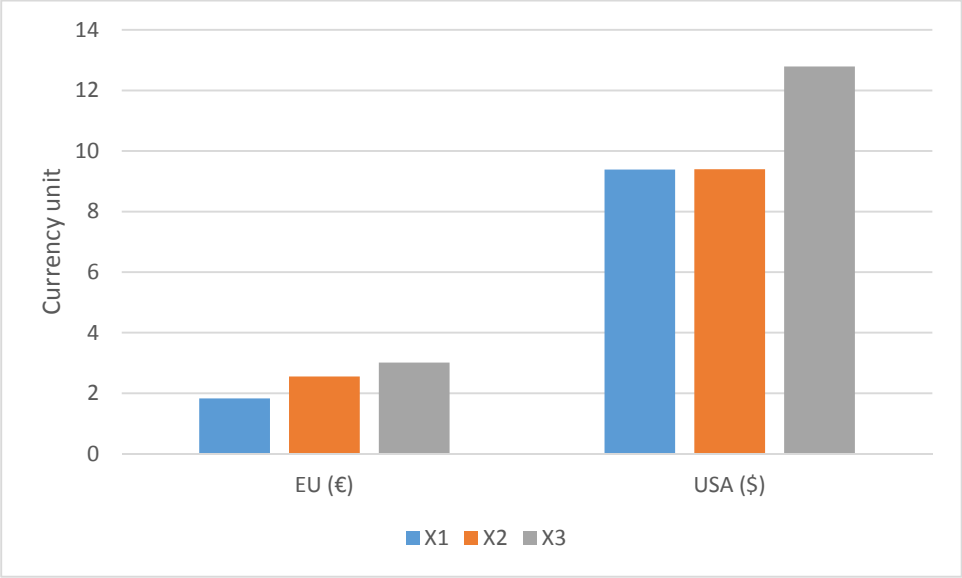
Overall the respondents (KOLs and payers) felt that the base case profile for Feraccru (superiority to placebo) was adequate but would prefer the data pertaining to upside profile for Feraccru (non-inferiority) vs IV iron, as would support the use in a broader patient population.

Pricing & Reimbursement analysis for Feraccru

The majority of respondents believe that the stated price for Feraccru was very reasonable, in particular when considering the cost savings that would be accrued not having to administer IV iron.

The conclusions on the Feraccru pricing expectations and potential was based on asking payers their unprompted price estimate for each of the TPPs presented (X1,X2,X3) and then revealing the actual daily price. Based on responses from a small but representative sample of payers across US and EU markets the following prices are deemed achievable.

Figure 10: Mean daily price expectation for Feraccru



Following on from this the reimbursement status for Feraccru was also considered and the upside profiles (non-inferiority to IV iron and/or superiority to IV iron) were favoured more that did X1 (supriority vs placebo) which was considered a minimum expectation for a new agent. (However, given the relatively small sample of payers interviewed GfK would recommend additional research to study further). All payes interviewed also felt that the Ferarrcu TPPs would be made available for formulary assessement within the year.

In conclusion, there is a potential place in the market for Feraccru (ST10) and all stakeholders (KOL, payers, and clinicians) felt it offers benefit over current treatment options. Feraccru has the potential to gain share in the iron products market, in patients who have recently failed on OFPs and patients who have already tried IV iron, but who will be switched onto Feraccru.

If Phase IIIb trials comparing Feraccru to IV iron supports the TPPs X2 (non-inferiority vs IV iron) and/or X3 (superiority to IV iron) then GfK predicts that Feraccru will appeal to a broader patient audience as well as achieving a higher price point than currently stated.

(Since Feraccru Phase IIIb trials are still ongoing, Shield Therapeutics cannot assure prospective investors that Feraccru will have the properties described in the TPPs X2/X3)

Situational analysis for PT20 (novel iron-based phosphate binder)

Hyperphosphataemia, that is, abnormally high serum phosphate levels, can result from increased phosphate intake, decreased phosphate excretion, or a disorder that shifts intracellular phosphate to extracellular space. However, even severe hyperphosphataemia is for the most part clinically asymptomatic. Morbidity In patients with this condition is more commonly associated with an underlying disease than with increased phosphate values and the most common cause of hyperphosphataemia is renal failure. Hyperphosphataemia is rare in the general population, but in patients with advanced chronic kidney disease, the rate of hyperphosphataemia is at least 70%. Almost all patients with dialysis-dependent kidney failure experience hyperphosphataemia at some time during the course of their disease. This is true for acute and chronic kidney disease.

Treatment for hyperphosphataemia generally includes the use of phosphate binders in late-stage CKD and dialysis patients but there is a high pill burden and high rates of adverse events with current therapies. This leads to poor adherence and reduced therapeutic benefit. Dialysis patients are far more likely than CKD-ND patients to be prescribed a phosphate binder, and are used in the majority of dialysis patients to control phosphate levels by preventing the absorption of phosphate.

Current therapies for the treatment of hyperphosphataemia are less than satisfactory and GfK's primary research with nephrologists indicated only a moderate degree of satisfaction with current phosphate binders with only the newer therapies (sevelamer and lanthanum) having higher levels of satisfaction, as they do not have the potential issues with causing hypercalcification that the calcium based binders have.

This suggests that there is a clear need for a treatment that can offer good efficacy in reducing phosphate levels, with few side effects and a low pill burden.

GfK believes that based on the current profile tested in the research, PT20 will have a more difficult task in differentiating itself in the market and may need to look to the outcome of forthcoming Phase 3 trials to emphasize its advantages from the other phosphate binders. Options also exist to position PT20 as a 'me-too' agent and/or by demonstrating its effectiveness with hard to treat (refractory) patients (although subject to Phase 2 study outcomes) to build a 'niche' strategy.

Reaction to PT20 amongst nephrologists and payers was positive and they felt that the key advantages of therapy was the potential of PT20 to offer iron supplementation in addition to lowering phosphate levels and so act as a combination treatment. This could lower pill burden for patients and reduce costs of IV iron and ESA.

Based on responses from nephrologists (pre/post allocation exercises), the majority stated that they would prescribe PT20 to at least some new patients and/or would switch patients from other therapies to PT20.

Pricing & Reimbursement analysis for PT20

Respondents were satisfied with the price comparator sevelamer as this was regarded as the standard of care amongst phosphate binders. According to GfK qualitative market research conducted, the potential price premium that could be expected for PT20 vs sevelamer based on the presented profile was 10-15%. Although future generic sevelamer entry may compromise the price potential for PT20 there are currently no generic sevelamer options on the market (only exception

being one released by Sanofi at a 10% discount) so the future impact of generics in this market remains uncertain and warrants further investigation.

In terms of reimbursement potential for PT20, payers were divided and stated that their decision would be dependent on efficacy and/or price i.e. if less expensive but similar efficacy to existing products then will be reimbursed and if it can demonstrate superior efficacy to existing products it will also be reimbursed at the higher price point.

In conclusion, there is a potential place in the market for PT20 but will be limited by fact that nephrologists did not perceive the current TPP presented to offer a significant competitive advantage over currently available products. In addition, the forthcoming generic entry of Renagel (sevelamer hydrochloride) and Renvela (sevelamer carbonate) may further compromise the price premium potential for PT20. Despite these challenges, PT20 could complement the portfolio offered to nephrologists by Shield Therapeutics given the fact that the same nephrologists will be approached by Feraccru sales representatives thereby providing an opportunity to 'up sell' PT20, with minimal incremental commercial investment.

GfK UK Ltd complies with the requirements of the international standard ISO 9001:2000 – Quality Assurance and ISO 20252 – Market, opinion and social research

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Appendix: Target Product Profiles for Feraccru (X1, X2 and X3)

Target Product Profile for Product X1

Indication	The treatment of iron-deficient anaemia in patients who cannot tolerate other oral iron preparations or are non-compliant
Formulation	Low dose (30mg elemental iron) oral formulation
Dosage	One 30mg tablet twice daily (i.e. morning and evening) swallowed on an empty stomach with water
Efficacy	Pivotal Phase 3 study showed Product X1 to be superior to placebo Mean increase in Hb levels of 2.3g/dL from baseline to week 12. • 78.1% of Product X1 subjects achieved at least an increase of 1g/dL from baseline Hb concentration at Week 12; 56.3% Product X subjects achieved increase of 2g/dL • 65.6% Product X1 subjects achieved normalised Hb concentration at Week 12 Open-label phase: mean ferritin and Hb levels continued to rise with Product X1 treatment
Adverse events	<5% treated patients withdrew from therapy • Most frequent AEs were GI symptoms – flatulence (4%); constipation (4%); abdominal discomfort (3%); distension (3%)
Drug interactions	No drug interaction studies performed. Food may inhibit uptake of Product X1
Contraindications	Haemochromatosis and other iron overload syndromes Patients receiving repeated blood transfusions

Target Product Profile for Product X2

Differences from TPP for X1 are highlighted in **red**

Indication	The treatment of iron-deficient anaemia in patients who cannot tolerate other oral iron preparations or are non-compliant
Formulation	Low dose (30mg elemental iron) oral formulation
Dosage	One 30mg tablet twice daily (i.e. morning and evening) swallowed on an empty stomach with water
Efficacy	Phase 3 study showed Product X2 to be **non-inferior to IV iron** Mean increase in Hb levels of 2.3g/dL from baseline to week 12. • 78.1% of Product X2 subjects achieved at least an increase of 1g/dL from baseline Hb concentration at Week 12; 56.3% Product X2 subjects achieved increase of 2g/dL • 65.6% Product X2 subjects achieved normalised Hb concentration at Week 12 Open-label phase: mean ferritin and Hb levels continued to rise with Product X2 treatment
Adverse events	<5% treated patients withdrew from therapy • Most frequent AEs were GI symptoms – flatulence (4%); constipation (4%); abdominal discomfort (3%); distension (3%)
Drug interactions	No drug interaction studies performed. Food may inhibit uptake of Product X2
Contraindications	Haemochromatosis and other iron overload syndromes Patients receiving repeated blood transfusions

Target Product Profile for Product X3

Differences from TPPs for X1 and X2 are highlighted in **red**

Indication	The treatment of iron-deficient anaemia in patients who cannot tolerate other oral iron preparations or are non-compliant
Formulation	Low dose (30mg elemental iron) oral formulation
Dosage	One 30mg tablet twice daily (i.e. morning and evening) swallowed on an empty stomach with water
Efficacy	Phase 3 study showed Product X3 to be **superior to IV iron** Mean increase in Hb levels of 2.3g/dL from baseline to week 12. • 78.1% of Product X3 subjects achieved at least an increase of 1g/dL from baseline Hb concentration at Week 12; 56.3% Product X3 subjects achieved increase of 2g/dL • 65.6% Product X3 subjects achieved normalised Hb concentration at Week 12 Open-label phase: mean ferritin and Hb levels continued to rise with Product X3 treatment
Adverse events	<5% treated patients withdrew from therapy • Most frequent AEs were GI symptoms – flatulence (4%); constipation (4%); abdominal discomfort (3%); distension (3%)
Drug interactions	No drug interaction studies performed. Food may inhibit uptake of Product X3
Contraindications	Haemochromatosis and other iron overload syndromes Patients receiving repeated blood transfusions

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Appendix: Target Product Profile for PT20

Target Product Profile for Product Y

Indication	The treatment and prevention of hyperphosphataemia in pre-dialysis and dialysis patients [Product Y is a phosphate binder indicated for the control of serum phosphate in patients with hyperphosphataemia. Product Y reduces the amount of intravenous iron and erythropoietin agents required in the management of iron-deficiency anaemia in patients receiving dialysis.]
Formulation	Oral tablet containing 800mg Product Y, including 200mg ferric iron
Dosage	New dialysis patients: Initial dose is 1 tablet with each meal Sevelamer switch patients: 2 tablets with each meal Maximum daily dose: 6 to 9 tablets (3 tablets per meal)
Efficacy	Phase 3 trial: 750 dialysis patients with hyperphosphataemia Product Y shown to be non-inferior vs. sevelamer over 52 wk period Iron absorption demonstrated – amount of IV iron needed to maintain Hb levels was reduced by 25%; EPO doses reduced by 15%
Adverse events	<10% patients discontinued Product Y because of treatment-related AEs AEs: Diarrhoea (15%); abdominal discomfort/pain (7%); nausea (7%); flatulence (5%)
Drug interactions	Product Y should be separated by at least 1 hour from certain antibiotics to avoid reduction in antibiotic absorption
Contraindications	Patients with iron overload diseases
Warnings and precautions	Hb levels should be routinely monitored. Other forms of administered iron and erythropoietin stimulating agents may need to be reduced

 4

PART 9

PARTICULARS OF THE WARRANTS

Pursuant to the Placing, Warrants are being issued to subscribers of Placing Shares on the basis of 7 Warrant for every 13 Placing Shares. Application will be made for the Warrants to be issued pursuant to the Placing to be admitted to trading on AIM. Set out below are the particulars of the principal terms and conditions applying to the Warrants constituted by an instrument entered into by the Company by way of deed poll dated 12 February 2016 (the "**Warrant Instrument**").

1 Constitution

1.1 The Company has determined by a resolution of the Board to issue 11,666,658 Warrants each entitling the holder thereof (the "**Warrantholder**") to subscribe for Ordinary Shares at 150p per Ordinary Share (or such adjusted price as may be determined from time to time in accordance with the provisions of the Warrant Instrument) (the "**Exercise Price**") payable in cash in full on subscription.

1.2 The Warrants registered in a Warrantholder's name may be held in certificated form (in which event they will be evidenced by a warrant certificate issued by the Company) or in uncertificated form.

1.3 The Warrants are issued subject to the Articles and, in the case of Warrants held in uncertificated form, the CREST Regulations and otherwise on the terms of the Warrant Instrument.

2 Subscription rights

2.1 The Warrantholder of each Warrant will have the right, subject to paragraph 2.2 below, which may be exercised on any business day from the date of the Warrant Instrument up to (and including) 30 June 2017 (the "**Expiry Date**"), being the period during which the Warrants may be exercised (the "**Subscription Period**"), to subscribe in cash for one Ordinary Share (subject to adjustment in accordance with the terms of the Warrant Instrument) in consideration of the payment of the Exercise Price in full per Warrant.

2.2 A Warrantholder shall be prohibited from exercising the rights to subscribe attaching to a Warrant if it would result in such exercising Warrantholder together with all persons with whom it is acting in concert triggering a requirement to make a mandatory offer under Rule 9 of the Takeover Code.

2.3 Every Warrant in respect of which subscription rights:

2.3.1 have been exercised in full; or

2.3.2 at the end of the Subscription Period have not been exercised,

shall lapse and be cancelled.

2.4 Ordinary Shares allotted pursuant to the exercise of Warrants in accordance with the terms of the Warrant Instrument shall be issued fully-paid and free from any liens, charges or encumbrances and rights of pre-emption but shall not rank for any dividends or other distributions declared, made or paid on the Ordinary Shares for which the record date is prior to the date on which the Warrants are exercised (the "**Exercise Date**") but, subject thereto, shall rank in full for all dividends and other distributions declared, made or paid on the Ordinary Shares on or after the Exercise Date and otherwise *pari passu* in all respects with the Ordinary Shares in issue at that date.

2.5 At any time when the Ordinary Shares are admitted to trading on AIM, application will be made by the Company to the London Stock Exchange for the Ordinary Shares allotted pursuant to any exercise of Warrants to be admitted to trading on AIM and the Company will use its reasonable endeavours to obtain such admission so as to be effective simultaneously with the allotment of the relevant Ordinary Shares pursuant to the exercise of the Warrants in accordance with the terms of the Warrant Instrument becoming effective.

3 Transfer and title

Warrants shall be transferable individually in the case of Warrants held in certificated form, by an instrument of transfer in any usual or common form or such other form as may be approved by or on behalf of the Company, and, in the case of Warrants held in uncertificated form, by a properly authenticated dematerialised instruction and/or other instruction or notification received by the Company or by such person as it may require for these purposes in such form and subject to such terms and conditions as may from time to time be prescribed by or on behalf of the Company (subject always to the facilities and requirements of the relevant system concerned).

4 Undertakings of the Company

4.1 The Company shall not in any way modify the rights attaching to the existing Ordinary Shares as a class in any way which operates to vary the rights of the Warrantholders in relation to the Warrants.

4.2 Warrantholders will have made available to them, at the same time and in the same manner as the same are made available to holders of Ordinary Shares, copies of the audited accounts of the Company (with the relevant directors' and auditor's reports) and copies of all other circulars or notices which are made available to holders of Ordinary Shares.

5 Adjustment of subscription rights

The Exercise Price shall from time to time be adjusted in accordance with the provisions of the Warrant Instrument for each of the following events giving rise to such adjustment (each an "**Adjustment Event**"):

5.1 *Consolidation or sub-division:* the Exercise Price shall be adjusted if and whenever the nominal value of the Ordinary Shares is altered as a result of consolidation or sub-division of the Ordinary Shares of the Company;

5.2 *Capitalisation of profits or reserves*: the Exercise Price shall be adjusted if and whenever the Company issues any Ordinary Shares credited as fully paid to the holders of Ordinary Shares by way of capitalisation of profits or reserves:

5.3 *Special Dividend*: the Exercise Price shall be adjusted if and whenever the Company pays or makes any Special Dividend to the holders of Ordinary Shares (except where the Exercise Price falls to be adjusted under paragraph 5.2 above);

5.4 *Capital Distribution*: The Exercise Price shall be adjusted if and whenever the Company pays or makes any Capital Distribution to holders of Ordinary Shares (except where the Exercise Price falls to be adjusted under subparagraphs 5.2, 5.3 or 5.5);

5.5 Rights issues to holders of Ordinary Shares: The Exercise Price shall be adjusted if and whenever the Company makes any offer or invitation to subscribe for new Ordinary Shares or for securities convertible into or exchangeable for Ordinary Shares or conferring rights to subscribe for Ordinary Shares (whether by way of rights issue, open offer or otherwise) to holders of Ordinary Shares (subject to such exclusions as may be necessary to deal with legal or regulatory requirements or restrictions in any jurisdiction) as a class on a pre-emptive basis at a consideration per Ordinary Share which is less than 95 per cent. of the Current Market Price of the Ordinary Shares on the Business Day immediately preceding the date of the first public announcement of the terms of such offer or invitation;

5.6 Whenever the Exercise Price is adjusted in accordance with the Warrant Instrument (other than by reason of a consolidation of the share capital of the Company as referred to in sub-paragraph 5.1 above) the number of Ordinary Shares for which a Warrantholder is entitled to subscribe shall be increased accordingly at the same time as such adjustment takes effect.

5.7 Whenever the Exercise Price is adjusted in accordance with the Warrant Instrument by reason of a consolidation of the share capital of the Company as referred to in sub-paragraph 5.1 above, the number of Ordinary Shares for which a Warrantholder is entitled to subscribe shall be decreased accordingly at the same time as such adjustment takes effect.

5.8 If and whenever the Company (in its sole discretion) determines that:

5.8.1 an adjustment should be made to the number of Ordinary Shares receivable upon exercise of a Warrant as a result of one or more events or circumstances not referred to in sub-paragraphs 5.1 to 5.5 (even if the relevant event or circumstance is specifically excluded from the operation of such clauses);

5.8.2 more than one event which gives rise or may give rise to an adjustment to the number of Ordinary Shares receivable upon exercise of a Warrant has occurred or will occur within such a short period of time that a modification to the operation of the adjustment provisions is required in order to give the intended result; or

5.8.3 one event which gives rise or may give rise to more than one adjustment to the number of Ordinary Shares receivable upon exercise of a Warrant has occurred or will occur such that a modification to the operation of the adjustment provisions is required in order to give the intended result,

then the Company shall, at its own expense, use its reasonable endeavours to procure that such adjustment (if any) to the number of Ordinary Shares receivable upon exercise of a Warrant as is fair and reasonable to take account thereof and the date on which such adjustment should take effect shall be determined by the appointed investment bank.

Upon such determination, the Company shall procure that such adjustment (if any) shall be made and shall take effect in accordance with such determination, provided, however, that an adjustment shall only be made pursuant to this clause if the appointed investment bank is requested to make such a determination not more than 30 calendar days after the date on which the relevant event occurs or circumstances exist.

5.9 The Exercise Price may not be reduced so that, on exercise of any Warrants, Ordinary Shares would fall to be issued at a discount to their nominal value.

5.10 No adjustment shall be made to the Exercise Price where such adjustment would be less than 1 per cent. of the Exercise Price then in effect. Any adjustment not required to be made pursuant to the preceding sentence shall be carried forward and included in any subsequent adjustment but such subsequent adjustment shall be made on the basis that the adjustment not required to be made had been made at the relevant time.

6 Takeovers

6.1 The Company shall notify the Warrantholders of the terms of any proposed Takeover Offer or Scheme at the same time as such terms are communicated to shareholders of the Company.

6.2 The Company shall notify the Warrantholders when any Takeover Offer becomes wholly unconditional, or Scheme becomes effective, at the same time as that fact is publicly announced or otherwise communicated to shareholders of the Company.

6.3 If a Takeover Offer becomes wholly unconditional, or a Scheme becomes effective, before the Expiry Date, the Company shall use its reasonable endeavours to procure that an appropriate offer (as such term is interpreted pursuant to Rule 15 of the Takeover Code ("**Rule 15**")) is extended to the holders of any remaining Warrants in accordance with Rule 15.

7 Winding up of the Company

7.1 If at any time prior to the Expiry Date an order is made or an effective resolution is passed for the winding up or dissolution of the Company or if any other dissolution of the Company by operation of law is to be effected:

7.1.1 if the winding up or dissolution is for the purposes of implementing a reconstruction, amalgamation or scheme of arrangement on terms previously sanctioned by an extraordinary resolution, such terms shall be binding on the Warrantholders; and

7.1.2 in any other case, the Company shall as soon as reasonably practicable send to the Warrantholders a written notice stating that such an order has been made or resolution has been passed or other dissolution is to be effected. Each Warrantholder may at any time within 60 days after the date of such notice elect, by written notice to the Company, to be treated as if he had, immediately before the date of the making of the order or the passing of the resolution or other dissolution, exercised some or all of his subscription rights. On giving such notice, a Warrantholder is entitled to receive out of

the assets which would otherwise be available in the liquidation to the shareholders of the Company such sum, if any, as he would have received had he been the holder of, and paid for, the Ordinary Shares to which he would have become entitled by virtue of that exercise, after deducting from that sum an amount equal to the aggregate Exercise Price which would have been payable by him upon such exercise.

7.2 Subject to compliance with paragraph 7.1, all Warrants shall lapse on liquidation of the Company.

8 Purchase and cancellation

8.1 The Company may at any time purchase Warrants:

8.1.1 by tender (available to all Warrantholders alike) at any price; or

8.1.2 on market; or

8.1.3 by private treaty at any price.

8.2 All Warrants purchased shall be cancelled forthwith and may not be reissued or sold.

9 Meetings of Warrantholders

9.1 Meetings of Warrantholders may be convened in accordance with the provisions of the Warrant Instrument and shall be competent to pass extraordinary resolutions of the Warrantholders and to exercise all the powers as referred to therein.

9.2 The expression ''extraordinary resolution'' means a resolution passed at a meeting of the Warrantholders and carried by a majority consisting of not less than 75 per cent. of the persons voting thereat upon a show of hands or, if a poll is duly demanded, by a majority consisting of not less than 75 per cent. of the votes given on such poll.

9.3 Without prejudice to the generality of the foregoing, the Warrantholders, by way of extraordinary resolution, shall have power to:

9.3.1 sanction any compromise or arrangement proposed to be made between the Company and the Warrantholders or any of them;

9.3.2 sanction any proposal by the Company for modification, abrogation, variation or compromise of, or arrangement in respect of the rights of the Warrantholders against the Company whether such rights shall arise under the Warrant Instrument or otherwise;

9.3.3 sanction any proposal by the Company for the exchange or substitution for the Warrants of, or the conversion of the Warrants into, shares, stock, bonds, debentures, debenture stock, warrants or other obligations or securities of the Company or any other body corporate formed or to be formed;

9.3.4 assent to any modification of the conditions to which the Warrants are subject and/or the provisions contained in the Warrant Instrument which shall be proposed by the Company;

9.3.5 authorise any person to concur in and execute and do all such documents, acts and things as may be necessary to carry out and give effect to any extraordinary resolution of the Warrantholders;

9.3.6 discharge or exonerate any person from any liability in respect of any act or omission for which such person may have become responsible under the Warrant Instrument; and

9.3.7 give any authority, direction or sanction which under the provisions of the Warrant Instrument is required to be given by extraordinary resolution of the Warrantholders.

10 Modifications to the Warrant Instrument

Any modification to the Warrant Instrument may be effected only by an instrument in writing, executed by the Company and expressed to be supplemental to the Warrant Instrument and, save in the ease of a modification which is of a formal, minor or technical nature or made to correct a manifest error, only if it shall first have been sanctioned by an extraordinary resolution of the Warrantholders.

PART 10

ADDITIONAL INFORMATION

1 Incorporation and activity of the Company

1.1 The Company was incorporated in England and Wales as a public limited company on 3 September 2015 with registered number 9761509.

1.2 The Company's registered office and principal place of business is at Northern Design Centre, Baltic Business Quarter, Gateshead Quays NE8 3DF. The Company's telephone number is +44 (0)191 511 8500.

1.3 On 1 October 2015, the Company was issued with a trading certificate under section 761 of the Act entitling it to commence business. The liability of members of the Company is limited.

1.4 The principal legislation under which the Company operates and under which the Ordinary Shares were created is the Act.

1.5 The principal activity of the Company is to act as the holding company for the Group.

2 Corporate Reorganisation

2.1 On 1 October 2015, the Company acquired the entire issued share capital of SHG in consideration for the issue of 46,271,210 ordinary shares of 1p each in the Company and 22,719,679 preference shares. On 5 October 2015, those preference shares were converted into 22,719,679 ordinary shares of 1p each in the Company pursuant to the special resolution referred to in paragraph 3.1.2(c) below.

2.2 On 12 February 2016, the Company issued one ordinary share of 1p in order to facilitate a sub-division and consolidation. On 12 February 2016 each of the ordinary shares of 1p each in the capital of the Company were sub-divided into two ordinary shares of 0.5p and, immediatedly thereafter, the ordinary shares of 0.5p each were consolidated into ordinary shares of 1.5p each on the basis of every three ordinary shares of 0.5p each being consolidated into one ordinary share of 1.5p each.

2.3 As part of the Corporate Reorganisation, W. Health exchanged (i) rights to acquire shares in SHG and (ii) rights to a preference amount, for an option to subscribe for 19,844,447 New Shares for an aggregate subscription price of €4,981,703 pursuant to the W. Health Replacement Option.

2.4 As part of the Corporate Reorganisation, IRORPH received the right to subscribe for 742,456 New Shares at nominal value of 1.5p per Ordinary Share pursuant to the IRORPH Top-up Option.

2.5 In preparation for Admission as part of the Corporate Reorganisation:

(a) W. Health has exercised the W. Health Replacement Option;

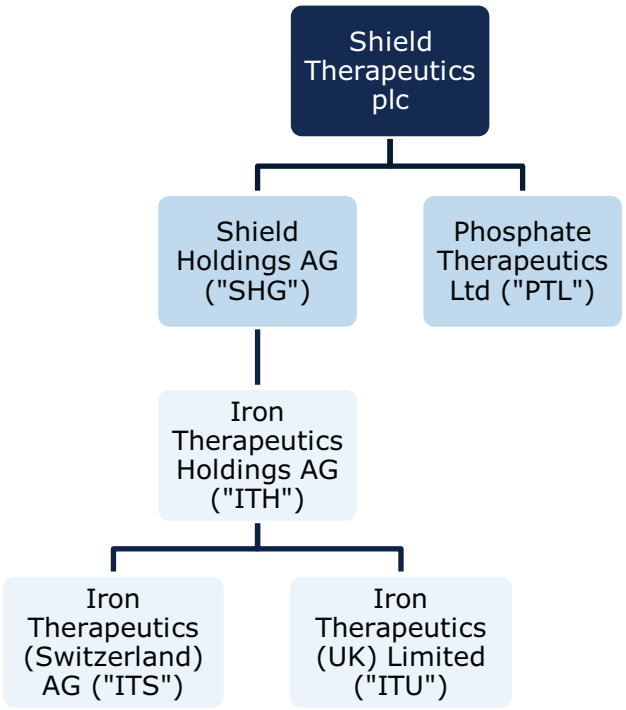
(b) IRORPH has exercised the IRORPH Top-up Option; and

(c) the Company has agreed to acquire the entire issued and to be issued share capital of PTL in consideration for the issue of 19,887,791 New Shares,

all of which are conditional upon, and will take effect upon, Admission.

The Corporate Reorganisation will result in the previous shareholders of SHG and PTL holding 77% and 23% of the issued share capital of the Company respectively, but before the issue of the Placing Shares.

2.5 The following chart reflects the Group's corporate structure upon Admission after completion of the Corporate Reorganisation:



All of the Company's subsidiaries will be wholly owned upon Admission.

Upon Admission, the Company will have two wholly owned direct subsidiaries, SHG and PTL.

SHG is focused on the development and commercialisation of one of the Group's key products, Feraccru. SHG has one wholly owned subsidiary, ITH. ITH owns the intellectual property related to Feraccru and has two wholly owned subsidiaries, ITS and ITU. ITS and ITU are the main trading companies of the Group which have been conducting the Group's clinical trials and which employ the Group's staff.

PTL is focused on the Group's other key product, PT20, together with the PT30 and PT40 development projects. It owns the licences in respect of certain patent rights and related know-how to develop and commercialise products for specific medical applications, including in relation to PT20.

3 Share capital

3.1 The share capital history of the Company is as follows:

3.1.1 On incorporation, two ordinary shares of £1.00 each in the Company were allotted and issued fully paid as subscriber shares to Carl Sterritt and Richard CM Jones in consideration for the payment of £2;

3.1.2 The following alterations in the issued share capital of the Company have taken place since incorporation:

(a) on 1 October 2015, pursuant to an ordinary resolution of the Company, each ordinary share of £1.00 each in the capital of the Company was sub-divided into 100 ordinary shares of 1p each;

(b) on 1 October 2015, an aggregate of 46,271,210 ordinary shares of 1p each and 22,719,679 preferred shares of 1p each were issued to the then shareholders of SHG pursuant to the share exchange agreement referred to in paragraph 9.7 of this Part 10 (*Additional Information*), in consideration for the transfer of the entire issued share capital of SHG to the Company. These shares were accordingly not paid up in cash;

(c) on 5 October 2015, pursuant to a special resolution of the Company passed on 1 October 2015, the 22,719,679 issued preferred shares of 1p each in the capital of the Company were converted into 22,719,679 ordinary shares of 1p each;

(d) on 12 February 2016, 1 ordinary share of 1p was issued in contemplation of the sub-division and consolidation outlined in paragraph (e) below;

(e) on 12 February 2016, pursuant to an ordinary resolution of the Company, each of the ordinary shares of 1p each in the capital of the Company has sub-divided into two ordinary shares of 0.5p each and, immediately thereafter, the ordinary shares of 0.5p each were consolidated into ordinary shares of 1.5p each on the basis of every three ordinary shares of 0.5p each being consolidated into one ordinary share of 1.5p;

(f) pursuant to the W. Health Replacement Option referred to in paragraph 9.8 of this Part 10 (*Additional Information*), which was exercised on 12 February 2016, 19,844,447 New Shares have been agreed to be issued to W. Health, conditional upon Admission, in consideration for the payment of €4,981,703;

(g) pursuant to the IRORPH Top-up Option referred to in paragraph 9.9 of this Part 10 (*Additional Information*), which was exercised on 12 February 2016, 742,456 New Shares have been agreed to be issued to IRORPH, conditional upon Admission, in consideration for the payment of £11,136.84;

(h) pursuant to the share exchange agreement referred to in paragraph 9.10 of this Part 10 (*Additional Information*), 19,887,791 New Shares have been agreed to be issued to the shareholders of PTL in consideration for the transfer of the entire issued and to be issued share capital of PTL to the Company, conditional upon Admission. These Ordinary Shares will accordingly not be paid up in cash; and

(i) pursuant to the Placing Agreement referred to in paragraph 13 of this Part 10 (*Additional Information*) and the Subscription Agreements referred to in paragraph 9.14 of this Part 10 (*Additional Information*) 21,666,662 New Shares and 11,666,658 Warrants have been agreed to be issued to certain existing Shareholders, institutional and other investors, conditional upon Admission.

3.2 The issued and fully paid share capital of the Company (a) as at the date of this document and (b) upon Admission, is and will be as follows:

(a) In issue at the date of this document		**(b) In issue upon Admission**	
Number of Ordinary Shares	**Nominal amount**	**Number of Ordinary Shares**	**Nominal amount**
45,994,060	£689,910.90	108,135,416	£1,622,031.28

As at 11 February 2016 (the latest practicable date prior to the date of this document), the Company held no treasury shares.

3.3 By resolutions passed on 12 February 2016:

3.3.1 each of the ordinary shares of 1p each in the capital of the Company were sub-divided into two ordinary shares of 0.5p each and, immediately thereafter, the ordinary shares of 0.5p each were consolidated into ordinary shares of 1.5p each on the basis of every three ordinary shares of 0.5p each being consolidated into one ordinary share of 1.5p;

3.3.2 new articles of association of the Company were adopted;

3.3.3 the Directors were generally and unconditionally authorised in accordance with section 551 of the Act to exercise all the powers of the Company to allot shares in the Company and/or grant rights to subscribe for or convert any security into such shares:

(a) up to an aggregate nominal amount of £300,000 in connection with the W. Health Replacement Option,

(b) up to an aggregate nominal amount of £12,000 in connection with the IRORPH Top-up Option; and

(c) up to an aggregate nominal amount of £300,000 in connection with the acquisition of PTL;

such authority to expire on the earlier of immediately following Admission and 31 March 2016, save that the Company may, at any time prior to the expiry of such authority, make an offer or enter into an agreement which would or might require the allotment of shares or the grant of rights to subscribe for or to convert any securities into shares in pursuance of such an offer or agreement as if such authority had not expired;

3.3.4 the Directors were generally empowered (pursuant to section 570 of the Act) to allot equity securities pursuant to the authority referred to in paragraph 3.3.3 above as if section 561 of the Act did not apply to any such allotment.

3.4 By resolutions passed on 12 February 2016:

3.4.1 new articles of association of the Company were adopted with effect from Admission;

3.4.2 the Directors were generally and unconditionally authorised in accordance with section 551 of the Act to exercise all the powers of the Company to allot shares in the Company and/or grant rights to subscribe for or convert any securities into such shares up to an aggregate nominal amount of £525,000 in connection with the issue of the Placing Shares and the Warrants, such authority to expire on the earlier of immediately following Admission and 31 March 2016, save that the Company may, at any time prior to the expiry of such authority, make an offer or enter into an agreement which would or might require the allotment of shares or the grant of rights to subscribe for or to convert any securities into shares in pursuance of such an offer or agreement as if such authority had not expired;

3.4.3 the Directors were generally empowered (pursuant to section 570 of the Act) to allot equity securities pursuant to the authority referred to in paragraph 3.4.2 above as if section 561 of the Act did not apply to any such allotment;

3.4.4 the Directors were generally and unconditionally authorised in accordance with section 551 of the Act to exercise all the powers of the Company to allot shares in the Company and/or grant rights to subscribe for or convert any securities into such shares up to an aggregate nominal amount of (A) £540,700 being equal to *1/3* of the Company's issued share capital immediately following Admission (such amount to be reduced by the nominal amount allotted or granted under part (B) of this resolution exceeding *1/3* of the Company's issued share capital immediately following Admission) and (B) £1,081,400 being equal to *2/3* of the Company's issued share capital immediately following Admission (such amount to be reduced by the nominal amount allotted or granted under part (A) of this resolution) in connection with an offer of such securities by way of a rights issue only, such authority to expire at the conclusion of the first annual general meeting of the Company, save that the Company may, at any time prior to the expiry of such authority, make an offer or enter into an agreement which would or might require the allotment of shares or the grant of rights to subscribe for or to convert any securities into shares in pursuance of such an offer or agreement as if such authority had not expired; and

3.4.5 the Directors were empowered (pursuant to section 570 of the Act) to allot equity securities as if section 561 of the Act did not apply to any such allotment or sale, (A) pursuant to the authorities granted in the above paragraph 3.4.4 above, in connection with a pre-emptive offer to holders of ordinary shares in proportion (as nearly as may be practicable) to their respective holdings (but in the case of the authorisation referred to in sub-paragraph (B) of paragraph 3.4.4 above, by way of a rights issue only), but subject to such other exclusions or other arrangements as the directors may consider necessary or appropriate to deal with fractional entitlements, record dates or legal, regulatory or practical difficulties which may arise under the laws of or the requirements of any regulatory body or stock exchange in any territory and (B) up to an aggregate nominal amount of £162,210, being equal to 10 per cent. of the Company's issued share capital immediately following Admission, such power to expire at the conclusion of the first annual general meeting of the Company, save that the Company may, at any time prior to the expiry of such power, make an offer or enter into an agreement which would or might require equity securities to be allotted after the expiry of such power, and the Directors may allot equity securities in pursuance of such an offer or an agreement as if such power had not expired.

3.5 The figure of 10 per cent. referred to in paragraph 3.4.5 above reflects the guidance from the Pre-Emption Group's revised Statement of Principles published on 12 March 2015 (the "**Statement of Principles**"). The Directors will have due regard to the Statement of Principles in relation to any exercise of this power, in particular (1) as regards to the allotment of the first 5 per cent., to the requirement for advance consultation and any explanation before making any non pre-emptive cash issue pursuant to this resolution which exceeds 7.5 per cent. of the share capital in any rolling three year period; and (2) as regards to the allotment of the second 5 per cent., the Directors confirm that they intend to use the power only in connection with an acquisition or specified capital investment (within the meaning of the Statement of Principles from time to time) which is announced contemporaneously with the issue, or which has taken place in the preceding six month period and is disclosed in the announcement of the issue.

3.6 In accordance with the authorities referred to in paragraphs 3.4.1 and 3.4.2 above, the New Shares were allotted pursuant to a resolution of the Board passed on 12 February 2016, conditional upon Admission.

3.7 The provisions of section 561 of the Act (which confer on Shareholders rights of pre-emption in respect of the allotment or sale of equity securities for cash) shall apply to any unissued share capital of the Company to the extent not disapplied pursuant to section 570 of the Act.

3.8 Save as disclosed in paragraph 3.1, since the date of its incorporation (i) there has been no alteration in the share capital of the Company (ii) no share or loan capital of the Company has been issued or agreed to be issued, or is now proposed to be issued for cash or any other consideration and (iii) no commissions, discounts, brokerages or other special terms have been granted by the Company in connection with the issue or sale of any such capital and no share or loan capital of the Company is under option or agreed, conditionally or unconditionally, to be put under option.

3.9 The Board considers the authorities and powers set out above to be appropriate in order to allow the Group flexibility to finance business opportunities or to conduct a pre-emptive offer or rights issue without the need to comply with the strict requirements of the statutory pre-emption provisions.

3.10 The Directors consider it desirable to have the maximum flexibility permitted by corporate governance guidelines to respond to market developments and to enable allotments to take place to finance business opportunities as they arise. There are no present plans to undertake a rights issue or to allot Ordinary Shares other than in connection with the Corporate Reorganisation, the Placing and Employee Incentive Schemes.

3.11 The Ordinary Shares and Warrants are in registered form and, subject to the provisions of the CREST Regulations, the Directors may permit the holding of shares in any class of shares in uncertificated form and title to such shares may be transferred by means of a relevant system (as defined in the CREST Regulations). Where Ordinary Shares and Warrants are held in certificated form, share certificates will be sent to the registered members by first class post.

4 AIM

Application will be made to the London Stock Exchange for the Ordinary Shares and Warrants to be admitted to trading on AIM. It is expected that Admission will become effective on an unconditional basis and that dealings in the Ordinary Shares and Warrants will commence trading on AIM by no later than 8.00 am on 26 February 2016.

Listing of the Ordinary Shares and Warrants is not being sought on any stock exchange other than AIM.

5 Articles of Association

A summary of the main provisions of the Articles is set out below.

5.1 Objects

The Articles do not provide for any objects of the Company and accordingly the Company's objects are unrestricted.

5.2 Variation of rights

Subject to the provisions of the Act and every other statute for the time being in force concerning companies and affecting the Company (the "**Statutes**"), if at any time the share capital of the Company is divided into different classes of shares, the rights attached to any class may be varied either with the consent in writing of the holders of three-quarters in nominal value of the issued shares of that class or with the sanction of a special resolution passed at a separate meeting of the holders of the shares of that class (but not otherwise) and may be so varied either whilst the Company is a going concern or during, or in contemplation of, a winding-up. At every such separate general meeting the necessary quorum shall be two persons holding or representing by proxy at least one-third in nominal value of the issued shares of the class in question (but at any adjourned meeting any holder of shares of the class present in person or by proxy shall be a quorum). Every holder of shares of the class present in person or by proxy shall, on a poll, have one vote in respect of every share of the class held by him and shall be entitled to demand a poll. Where the rights of some only of the shares of any class are to be varied, the foregoing provisions apply as if each group of shares of the class differently treated formed a separate class whose rights are to be varied.

5.3 Alteration of share capital

The Company may, subject to the passing of a resolution authorising it to do so in accordance with the Act:

5.3.1 consolidate and divide all or any of its share capital into shares of a larger nominal amount than its existing shares;

5.3.2 subject to the provisions of the Act, sub-divide its shares, or any of them, into shares of smaller nominal amount than its existing shares; and

5.3.3 determine that, as between the holders of the shares resulting from such a sub-division, one or more shares may have such preferred or other rights or may have such qualified or deferred rights or may be subject to such restrictions, as compared with the other or others, as the Company has power to attach to new shares.

5.4 Issue of shares

Subject to the provisions of the Act and the rights attaching to any existing shares, any share may be issued with, or have attached to it, such rights or restrictions as the Company may by ordinary resolution determine or, if the Company has not so determined, as the Directors may determine.

5.5 Dividends and other distributions

Subject to the provisions of the Act and the Articles, the Company may by ordinary resolution declare dividends to be paid to shareholders in accordance with their respective rights and interests in the profits of the Company. However the dividends shall not exceed the amount recommended by the Directors. Subject to the provisions of the Act and, so far as in the opinion of the Board the profits justify such payments, the Directors may declare and pay interim dividends, or fixed dividends payable as the Board sees fit.

Subject to the rights of persons (if any) entitled to shares with special rights as to dividend, all dividends shall be declared and paid according to the amounts paid up on the shares in respect of which the dividend is paid. If any share is issued on terms providing that it shall rank for dividend as if paid up (in whole or in part) from a particular date, such share shall rank for dividend accordingly. In any other case, dividends shall be apportioned and paid according to the amounts paid up on the shares during any portion or portions of the period in respect of which the dividend is paid.

5.6 Voting rights

Subject to any rights or restrictions attached to any shares, on a show of hands every shareholder present in person has one vote, every proxy present who has been duly appointed by one or more shareholders entitled to vote has one vote and every corporate representative present who has been duly authorised by a corporation has the same voting rights as the corporation would be entitled to.

On a poll every shareholder (whether present in person or by duly appointed proxy or corporate representative) has one vote for every share of which he is the holder or in respect of which his appointment as proxy or corporate representative has been made. A shareholder entitled to more than one vote need not, if he votes, use all his votes or cast all the votes he uses the same way. In the case of joint holders, only the vote of the most senior joint holder shall count (to the exclusion of the other joint holders), and seniority shall be determined by the order in which the names of the holders stand in the register of members of the Company.

No member shall be entitled to vote at any general meeting or meeting of the holders of any class of shares of the Company either personally or by proxy or to exercise any other right conferred by membership in relation to meetings of the Company or of the holders of any class of shares of the Company if any call or other sum then payable by him in respect of that share remains unpaid to the Company in respect of such shares remain unpaid.

5.7 Transfer of shares

A share in the Company in certificated form shall be transferred by instrument of transfer in any usual or common form, or in any other form approved by the Directors, signed by or on behalf of the transferor and, in the case of party paid shares, by or on behalf of the transferee.

All transfers of shares in uncertificated form shall be made in accordance with and be subject to the CREST Regulations and the facilities and requirements of the Relevant Electronic System concerned and in accordance with any arrangements made by the Board pursuant to the Articles.

The Directors may, in their absolute discretion, refuse to register the transfer of a share which is not fully paid provided that such refusal does not prevent dealings in the shares of that class from taking place on an open and proper basis. The Directors may also refuse to register a transfer of a share in certificated form unless the instrument of transfer:

- is duly stamped or duly certificated;
- is delivered for registration at the registered office of the Company or such other place as the Directors may appoint and is accompanied by the certificate for the share to which it relates and such other evidence as the Directors may reasonably require to show the right of the transferor to make the transfer;
- is in respect of only one class of share;
- is not in favour of more than four transferees; and
- is for a share which the Company has no lien.

The Directors may refuse to register a transfer of a share in uncertificated form in any case where the Company is entitled to refuse to register the transfer in such other circumstances as may be permitted by the CREST Regulations and the requirements of the Relevant Electronic System.

If the Directors refuse to register a transfer of a share, they shall send the transferee notice of the refusal within two months after the date on which the transfer was lodged with the Company or, in the case of an uncertificated share, the date on which the appropriate instruction was received by or on behalf of the Company in accordance with the CREST Regulations.

No fee shall be charged for the registration of any instrument of transfer or other document or instruction relating to or affecting the title to any share.

5.8 Distribution of assets on a winding-up

If the Company shall be wound up the liquidator may, with the sanction of a special resolution and with any other sanction required by the Insolvency Act 1986, divide among the shareholders in specie or kind the whole or any part of the assets of the Company and for such purpose may set such value as he sees fair upon any assets and may determine how such division shall be carried out as between the shareholders or different classes of shareholders. With the like sanction, the liquidator may vest the whole or any part of the

assets in trustees upon such trusts for the benefit of the shareholders as he shall think fit, but no shareholder shall be compelled to accept any shares or other securities upon which there is a liability.

5.9 Restrictions on rights: failure to respond to a section 793 notice

If a Shareholder, or any other person appearing to be interested in any shares held by that Shareholder, fails to provide the information requested in a notice given to him under section 793 of the Act by the Company in relation to his interest in shares (the "**default shares**") within 14 clear days after the notice has being given, the following restrictions shall apply:

Where the nominal value of the default shares represent at least 0.25 per cent. of their class, the holder of the default shares shall not be entitled:

- to attend or vote (whether in person or by representative or proxy) at any general meeting or annual general meeting of the Company;
- to receive any dividend or other distribution; or
- to transfer or agree to transfer any of the shares or rights in them.

The restrictions shall continue for the period specified by the Board, being not more than seven clear days after the earlier of:

- the Company being notified that the default shares have been sold pursuant to an exempt transfer (an exempt transfer being a sale of the share on a recognised investment exchange as defined in FSMA in the UK or on any stock exchange outside the UK on which those shares are listed or normally traded, a sale of the whole beneficial interest in the share or an acceptance of a takeover offer); or
- due compliance, to the satisfaction of the Board, with the section 793 notice.

The Board may waive these restrictions, in whole or in part, at any time.

5.10 Untraced shareholders

Subject to certain notice requirements, the Company shall be entitled to sell at the best price reasonably obtainable at the time of sale any share held by a shareholder if and provided that, during a period of 12 years, at least three cash dividends have been declared in respect of the share in question and all dividend warrants and cheques have been sent by the Company in accordance with the Articles and, during that period of 12 years, no cash dividend payable in respect of the share has been claimed by presentation to the paying bank of the relevant cheque or warrant, or been satisfied by the transfer of funds to a bank account designated by the member or person entitled by transmission and no communication has been received by the Company from the shareholder or the person entitled by transmission to the share.

5.11 Directors

Unless the Company determines otherwise by ordinary resolution, the number of Directors (other than alternate Directors) shall not be subject to any maximum but shall not be less than two.

Subject to the Articles, the Company may by ordinary resolution appoint any person to be a Director either to fill a casual vacancy or as an additional Director. Any Director so appointed shall retire at the Company's next annual general meeting and shall then be eligible for re-election.

Any Director may appoint any other Director, or any other person approved by the Board to be his alternate and may remove such alternate and appoint another in his place.

The business of the Company shall be managed by the Directors who, subject to the Act, the provisions of the Articles and any directions of the Company may exercise all the powers of the Company.

No business shall be transacted at any meeting of the Directors unless a quorum is present and unless otherwise determined, two directors shall be a quorum. A Director shall not be counted in the quorum present in relation to a matter or resolution on which he is not entitled

to vote but shall be counted in the quorum present in relation to all other matters or resolutions considered or voted on at the meeting. An alternate Director who is not himself a Director shall, if his appointor is not present, be counted in the quorum.

Questions arising at a meeting of the Directors shall be decided by a majority of votes. In the case of an equality of votes, the chairman of the meeting shall have a second or casting vote.

Subject to any other provision of the Articles, a Director shall not vote at a meeting of the Directors on any resolution concerning a matter in which he has, directly or indirectly, a material interest (other than an interest in shares, debentures or other securities of, or otherwise in or through, the Company) and which may give rise to a conflict of interests, unless his interest arises only because the case falls within certain limited categories specified in the Articles.

Each Director must declare any situation in which he has or can have a direct or indirect interest which conflicts (or may conflict) with the interests of the Company which, if not authorised would amount to a breach of section 175 of the Act (a "**conflict**").

For the purposes of section 175 of the Act, the Board may authorise any matter proposed to it in accordance with the Articles which would, if not so authorised, involve a breach of duty by a Director under that section, including, without limitation, any matter which relates to a situation in which a Director has, or can have, an interest which conflicts, or possibly may conflict, with the interests of the Company. Any such authorisation will be effective only if (a) the meeting at which the matter is considered is quorate without counting the Director in question or any other interested Director; and (b) the matter was agreed to without the interested Director voting or, if the Director did vote, would have been passed if their vote was not counted.

The Board may (whether while authorising or subsequently) make any such authorisation subject to any conditions or limits it expressly imposes but such authorisation is otherwise given to the fullest extent permitted. The Board may terminate or vary such authorisation at any time.

5.12 Indemnity

Subject to the provisions of, and so far as is permitted by and consistent with the Act, every Director, company secretary or other officer of the Company shall be indemnified out of the assets of the Company against (a) any liability incurred by or attaching to him in connection with any negligence, default, breach of duty or breach of trust by him in relation to the Company or any associated body; and (b) any other liability incurred by or attaching to him in the actual or purported execution and/or discharge of his duties and/or the exercise or purported exercise of his powers and/or otherwise in relation to or in connection with his duties, powers or office.

To the extent permitted by law, the Directors may arrange insurance cover at the cost of the Company in respect of any liability, loss or expenditure incurred by any Director, the company secretary, or other officer or auditor of the Company in relation to anything done or omitted to be done or alleged to have been done or omitted to be done as Director, company secretary, officer or auditor.

5.13 General Meetings

In the case of the annual general meeting, at least 21 clear days' notice shall be given to all the members and to the auditors. All other general meetings shall be convened by not less than 14 clear days' notice in writing.

No business shall be transacted at any general meeting unless a quorum is present. Two persons entitled to vote upon the business to be transacted, each being a shareholder or a proxy for a shareholder or a duly authorised representative of a corporation (including for this purpose two persons who are proxies or corporate representatives of the same shareholder), shall be a quorum.

A member may appoint a proxy to act on his behalf. A proxy need not be a member of the Company. The appointment of a proxy to vote at a meeting shall be deemed to confer authority to demand or join in demanding a poll and to vote on any resolution put to the meeting as the proxy thinks fit and shall be deemed to confer the right to speak at a meeting.

A member may appoint more than one proxy to attend on the same occasion and if he does so he shall specify the number of shares held by him in respect of which each proxy is entitled to exercise his rights. Multiple proxies may be appointed provided that each proxy is appointed to exercise the rights attached to a different share.

Any corporation which is a member of the Company may, by resolution of its directors or other governing body, authorise such person as it thinks fit to act as its representative at any meeting of the Company, or at any meeting of any class of members of the Company.

The appointment of a proxy shall not preclude a member from attending and voting in person at the meeting at a show of hands or on the poll concerned.

A Director shall, notwithstanding that he may not be a member of the Company, be entitled to attend and speak at general meetings or separate meetings of the holders of any class of shares.

Every resolution submitted to a general meeting shall be determined in the first instance by a show of hands of the members present in person by proxy or by corporate representative. However, subject to the provisions of the Statutes, a poll may be demanded (before or upon the declaration of the result of the show of hands) by (a) the chairman of the meeting; (b) not less than five members having the right to vote at the meeting; (c) a member or members representing not less than one-tenth of the total voting rights of all the members having the right to vote at the meeting; or (d) a member or members holding shares conferring a right to vote at the meeting, being shares on which an aggregate sum has been paid up equal to not less than one-tenth of the total sum paid up on all the shares conferring that right.

6 Subsidiary undertakings

Following completion of the Corporate Reorganisation, the Company will be the holding company of the Group and the Group will comprise of the Company and its subsidiary undertakings named below, all of which will be directly or indirectly 100 per cent. owned by the Company.

Name	Country of incorporation	Registered office	Principal activity
Phosphate Therapeutics Ltd	England and Wales	Northern Design Centre, Baltic Business Quarter, Gateshead Quays, Tyne and Wear NE8 3DF	Owns the licences in respect of certain patent rights and related know-how in relation to PT20
Shield Holdings AG	Switzerland	Sihleggstrasse 23, 8832 Wollerau, Switzerland	Holding company of the SHG Group
Iron Therapeutics Holdings AG	Switzerland	Sihleggstrasse 23, 8832 Wollerau, Switzerland	Owns the intellectual property relating to Feraccru
Iron Therapeutics (Switzerland) AG	Switzerland	Sihleggstrasse 23, 8832 Wollerau, Switzerland	Swiss operating subsidiary
Iron Therapeutics (UK) Limited	England and Wales	Northern Design Centre, Baltic Business Quarter, Gateshead Quays, Tyne and Wear NE8 3DF	UK operating subsidiary and main trading company of the Group

7 Interests of Directors, senior management, major shareholders and related party transactions

7.1 The interests of the Directors in the share capital of the Company were as at 11 February 2016, being the latest practicable date prior to the date of this document, and upon Admission are expected to be, as follows:

Name	Number of Ordinary Shares at 12 February 2016	Percentage of issued ordinary share capital at 12 February 2016	Number of Ordinary Shares upon Admission[1]	Percentage of issued ordinary share capital upon Admission[1]
Dr Andrew Heath	—	—	85,719	0.08
Carl Sterritt[2][4]	9,331,333	20.29	10,053,113[3]	9.30[3]
Richard CM Jones	886,774	1.93	1,448,990	1.34
James Karis	—	—	—	—
Peter Llewellyn-Davies	—	—	—	—

(1) Includes Ordinary Shares to be issued upon Admission in connection with the Corporate Reorganisation and pursuant to the Placing.

(2) Mr Sterritt will also hold 376,921 Warrants upon Admission, representing 3.2 per cent. of the Warrants in issue. This figure includes 269,230 Warrants which IRORPH has directed should be allotted to Mr Sterritt rather than IRORPH pursuant to the Subscription.

(3) Mr Sterritt has agreed to transfer 345,000 Ordinary Shares to IRORPH, conditional upon Admission, and accordingly these figures are reduced to take account of this transfer.

(4) Mr Sterritt has a call option over 345,000 Ordinary Shares which will be held by IRORPH upon Admission. This call option is exercisable during the twelve month period following expiry of the exercise period of the Warrants, at the aggregate price of £1 in the event that none of the Warrants are exercised. To the extent that Warrants are exercised, the number of Ordinary Shares subject to the option reduces on a sliding scale, with no Ordinary Shares being subject to the option if all of the Warrants are exercised.

7.2 There are no share options/awards expected to be held by the Directors upon Admission under the Company's new share incentive arrangements.

7.3 Save as disclosed in this paragraph 7, immediately following Admission, no Director will have any interest, whether beneficial or non-beneficial, in the share capital of the Company.

7.4 On 12 February 2016 each of the non-Executive Directors entered into letters of appointment with the Company. On 12 February 2016 each of the Executive Directors entered into new service agreements with the Company. The letters of appointment and service agreements are conditional upon Admission.

7.5 Executive Directors

7.5.1 On 12 February 2016, the Company entered into a service agreement with Carl Sterritt as Chief Executive Officer conditional upon Admission. The annual base salary payable to Mr Sterritt is £295,000 subject to review by the Remuneration Committee. He is also entitled to an annual car allowance of £12,000 and pension contributions equal to 12% of his base salary. In addition to the normal bank and public holidays, Mr Sterritt is entitled to 30 days' paid holiday each holiday year.

7.5.2 On 12 February 2016, the Company entered into a service agreement with Richard Jones as Chief Financial Officer conditional upon Admission. The annual base salary payable to Mr Jones is £215,000, subject to review by the Remuneration Committee. He is also entitled to an annual car allowance of £12,000 and pension contributions equal to 12% of his base salary. In addition to the normal bank and public holidays, Mr Jones is entitled to 29 days' paid holiday each holiday year to be increased to 30 days in April 2016 upon reaching five years of statutory continuous employment.

7.5.3 Carl Sterritt and Richard Jones may be eligible to participate in any incentive or similar plan operated by the Company, subject to the rules of any such plan. They are eligible for discretionary bonuses of up to one times salary. They will also receive a discretionary bonus of up to one times annual salary in respect of the financial year

ending 31 December 2015. Each of Mr Sterritt and Mr Jones are also each entitled to certain benefits, including life assurance cover, critical illness cover and income protection insurance.

7.5.4 Mr Sterritt and Mr Jones are subject to confidentiality restrictions without limitation in time, and restrictive covenants including non-competition, non-interference, non-solicitation and non-dealing restrictions. Both Mr Sterritt's and Mr Jones' restrictions are for a period of 12 months post termination of employment and may be reduced by any time spent on garden leave.

7.5.5 The service agreements of Mr Sterritt and Mr Jones may be terminated by either party by twelve months' written notice.

7.5.6 The Company may terminate each of the service agreements by making a payment in lieu of notice.

7.5.7 The Company may terminate Mr Sterritt's or Mr Jones' employment with immediate effect and without notice, pay in lieu of notice, or payment of any compensation or liquidated damages, if it has reasonable grounds to believe that Mr Sterritt or Mr Jones is guilty of any of the following non-exhaustive examples of behaviour or conduct, in summary: (i) any repeated breach of the service agreement after warning from the Company; or (ii) financial dishonesty; or (iii) gross or serious misconduct or wilful neglect in the discharge of his duties under his service agreement; or (iv) acting in any manner which is likely to bring him or the Company or any Group Company into disrepute or prejudice the interests of the Company or any Group Company; or (v) continuing unsatisfactory conduct or performance of his duties, after having received a warning from the Company relating to the same; or (vi) being convicted of any criminal offence (except a road traffic offence not involving a custodial sentence); or (vii) becoming of unsound mind or an in-patient for the purpose of any statute relating to mental health; or (viii) becoming bankrupt, applying for a bankruptcy petition or having a bankruptcy order made against him, or similar provisions in relation to a receiving order or interim order made against him under the relevant law; or (ix) being disqualified from holding office in the Company, any Group Company or any other company under the Insolvency Act 1986 or the Company Directors Disqualification Act 1986 or the FCA, or any equivalent procedure under relevant local law, or any professional or other body, which undermines the confidence of the Board in his continued employment with the Company; or (x) failing to comply in any material respect with any policy of the Company or any Group Company which has been communicated to him; or (xi) ceasing by reason of his own act or default to be a director of the Company or any Group Company; or (xii) entering into any transaction or behaving in any other way which constitutes an offence for the purposes of Part V of the Criminal Justice Act 1993 or which constitutes market abuse for the purposes of Part VIII of FSMA; or (xiii) committing any material breach of his duties as a director under Part 10 of the Act.

7.6 Non-Executive Directors

7.6.1 Dr Andrew Heath has been appointed as Non-Executive Chairman of the Board, by a letter of appointment, conditional on Admission. Dr Heath is entitled to an annual fee of £100,000. James Karis and Peter Llewellyn-Davies have been appointed as Non-Executive Directors of the Company by a letter of appointment, conditional on Admission. The Non-Executive Directors are each entitled to an annual fee of £36,000. The Non-Executive Director serving as Chair of the Audit Committee shall be entitled to a further annual fee of £8,000. The Non-Executive Director serving as Chair of the Remuneration Committee shall each be entitled to a further annual fee of £5,000. The Company may reimburse the Non-Executive Directors for all properly documented expenses reasonably incurred in the performance of their duties.

7.6.2 The appointments of the Non-Executive Directors are for an initial term of three years commencing on the date of Admission, unless terminated earlier by either party giving to the other three months prior written notice.

7.6.3 The Company may terminate the appointment with immediate effect if a Non-Executive Director has: (i) committed a material breach of obligations under the appointment letter; or (ii) committed any serious or repeated breach or non-observance of

obligations to the Company (which include an obligation not to breach statutory, fiduciary or common-law duties); or (iii) been guilty of any fraud or dishonesty or acted in any manner which, in the opinion of the Company, brings or is likely to bring the Non-Executive Director or the Company into disrepute or is materially adverse to the interests of the Company; or (iii) been convicted of an arrestable criminal offence, other than an offence under road traffic legislation in the United Kingdom or elsewhere for which a fine or non-custodial penalty is imposed; or (iv) been declared bankrupt or have made an arrangement with or for the benefit of his creditors, or if he has a county court administration order made against him under the County Court Act 1984; or (v) been disqualified from acting as a director; or (vi) been removed from office by the Company in accordance with the Articles; or (viii) not complied with the Company's anti-corruption and bribery policy and procedures or the Company's share dealing code.

7.7 The Company has not made any loans to the Directors or senior management of the Group which are outstanding, nor has it ever provided any guarantees for the benefit of any Director (or the Directors collectively) or senior management of the Group.

7.8 Over the five years preceding the date of this document, the Directors hold or have held the following directorships (apart from their directorships of any member of the Group) or memberships of the following administrative, management or supervisory bodies and/or partnerships:

Name	Current	Previous
Dr Andrew Heath	Oxford Biomedica plc Novacyt SA Integrated Healing Technologies, LLC XL Technologies LLC Carlyle Mansions (Tenants) Limited Carlyle Mansions Limited	Anew Optics Inc. Morvus Technology Limited Adjuvantix Bioindustry Association 22-24 Sloane Gardens Limited
Carl Sterritt	Envoda Limited Krysto Pharma Limited Hamm Court Limited	
Richard CM Jones ACA	Krysto Pharma Limited	Wolverleigh Consultants Ltd
James Karis	CollabRx, Inc DATATRAK International, Inc. Schuman IRB Mapi Développement SAS Mapi SAS Mapi Limited Mapi B.V. Mapi Canada, Inc. Mapi USA, Inc. Mapi Life Sciences Australia Pty Ltd Mapi Life Sciences Canada Inc. Mapi Life Sciences France SAS Mapi Life Sciences (Germany) GmbH Mapi Ireland Limited Mapi Italy S.r.l. Mapi Korea LLC Mapi Life Sciences NL B.V. Mapi Life Sciences Poland sp. z.o.o Mapi Life Sciences Singapore Pte. Ltd.	Marina Biotech, Inc

Name	Current	Previous
	Optum Spain Life Sciences, S.L.U. Mapi Sweden A.B. Mapi Life Sciences Singapore Pte. Ltd., Taiwan Branch Mapi Life Sciences UK Limited Mapi Life Sciences USA, Inc.	
Peter Llewellyn Davies	Medigene AG Medigene Inc Catherex Inc Aettis Inc Medigene Immunotherapies GmbH	WILEX AG WILEX Inc. Immunocore Ltd

7.9 None of the Directors or members of the Senior Management have in the five years before the date of this document:

- has any unspent convictions in relation to indictable offences; or
- has been bankrupt or the subject of an individual voluntary arrangement, or has had a receiver appointed to any asset of such director; or
- has been a director of any company which, while he or she was a director or within 12 months after he or she ceased to be a director, has a receiver appointed or went into compulsory liquidation, creditors voluntary liquidation, administration or company voluntary arrangement, or made any composition or arrangement with its creditors generally or with any class of its creditors; or
- has been a partner of any partnership which, while he or she was a partner or within 12 months after he or she ceased to be a partner, went into compulsory liquidation, administration or partnership voluntary arrangement, or has a receiver appointed to any partnership asset;
- has had any public criticisms of such director by statutory or regulatory authorities (including recognised professional bodies); or
- has been disqualified by a court from acting as a director of a company or from acting in the management or conduct of the affairs of any company.

7.10 In so far as is known to the Directors, the following are the interests (with the meaning of Part VI of the Act) (other than interests held by the Directors) which represent, or will represent, directly or indirectly, 3 per cent. or more of the issued share capital of the Company (being the threshold for notification of interests that applies to the Company and Shareholders, as of Admission, pursuant to Chapter 5 of the Disclosure and Transparency Rules) on 11 February 2016, being the latest practicable date prior to the date of this document:

	As at 11 February 2016		Immediately following Admission	
Name	**Number of Ordinary Shares**	**Percentage of issued ordinary share capital**	**Number of Ordinary Shares**	**Percentage of issued ordinary share capital[1]**
W. Health	15,146,452	32.9	54,062,901	49.99
IRORPH	9,609,752	20.9	12,563,874[5]	11.62
Christian Schweiger[2][4]	6,369,126	13.9	5,625,411[3]	5.20[3]
JP Morgan Asset Management (UK) Limited	—	—	4,000,000	3.70
Aviva Investors Global Services Limited	—	—	4,000,000	3.70

(1) Includes Ordinary Shares issued upon Admission in connection with the Corporate Reorganisation and pursuant to the Placing.

(2) Mr Schweiger will also hold 305,128 Warrants upon Admission, representing 2.6 per cent. of the Warrants in issue. This figure includes 269,231 Warrants which IRORPH has directed should be allotted to Mr Schweiger rather than IRORPH pursuant to the Subscription.

(3) Mr Schweiger has agreed to transfer 866,666 Ordinary Shares to IRORPH, conditional upon Admission, and accordingly these figures are reduced to take account of this transfer.

(4) Mr Schweiger has a call option over 866,666 Ordinary Shares which will be held by IRORPH upon Admission. This call option is exercisable during the twelve month period following expiry of the exercise period of the Warrants, at the aggregate price of £1 in the event that none of the Warrants are exercised. To the extent that Warrants are exercised, the number of Ordinary Shares subject to the option reduces on a sliding scale, with no Ordinary Shares being subject to the option if all of the Warrants are exercised.

(5) These figures include 1,211,666 Ordinary Shares IRORPH have agreed to acquire from Carl Sterritt and Mr Schweiger, conditional upon Admission. These Ordinary Shares are under option as referred to in footnote (4) above and footnote (4) to the table contained in paragraph 7.1 above.

7.11 In so far as it is known to the Directors, the following are the interests (within the meaning of Part VI of the Act) (other than interests held by the Directors) which represent, or will repsent, directly or indirectly, 3 per cent. or more of the issued warrant capital of the Company on 12 February 2016, being the last practicable date prior to the date of this document and immediately following Admission:

	As at 12 February 2016		Immediately following Admission	
Name	**Number of Warrants**	**Percentage of Warrants**	**Number of Warrants**	**Percentage of Warrants**
JP Morgan Asset Management (UK) Limited	—	—	**2,153,846**	18.46
Aviva Investors Global Services Limited	—	—	**2,153,846**	18.46
W. Health L.P.	—	—	**1,945,640**	16.68
Blackrock Investment Management (UK), Ltd	—	—	**1,457,435**	12.49
USS Investment Management Ltd	—	—	**1,435,897**	12.31
Hargreave Hale Limited	—	—	**1,076,923**	9.23
Carl Sterritt	—	—	**376,921**	3.23

7.12 All Shareholders have the same voting rights in respect of the share capital of the Company.

7.13 The Company and the Directors are not aware of any arrangements, the operation of which may at a subsequent date result in a change in control of the Company.

7.14 None of the Directors nor any members of a Director's family is dealing in any related financial product (as defined in the AIM Rules) whose value in whole or in part is determined directly or indirectly by reference to the price of the Ordinary Shares, including a contract for differences or a fixed odds bet.

7.15 Save:

7.15.1 as described in the SHG's Historical Financial Information for the three years and six months ended 30 June 2015 set out in note 26 to Part 5 (*Historical Financial Information for SHG*);

7.15.2 as described in PTL's Historical Financial Information for the three years and six months ended 30 June 2015 set out in note 21 to Part 6 (*Historical Financial Information for Phosphate Therapeutics*);

7.15.3 pursuant to the Corporate Reorganisation and the other transactions described in paragraphs 9.4, 9.5, 9.6, 9.7, 9.8, 9.9 and 9.10 of this Part 10 (*Additional Information*);

7.15.4 for the Relationship Agreement described in paragraph 11 of Part 1 (*Key Information and Details of the Placing*);

7.15.5 for the Distribution Agreement summarised in paragraph 9.2 of this Part 10 (*Additional Information*); and

7.15.6 the participation of IRORPH, W. Health and Carl Sterritt in the Placing.

there were no related party transactions entered into by the Company or any member of the Group during the three years and six months ended 30 June 2015 and during the period to 11 February 2016 (being the latest practicable date prior to the publication of this document).

8 Employee Incentive Schemes

8.1 The Shield Therapeutics plc 2016 Long-Term Incentive Plan

8.1.1 The Company adopted The Shield Therapeutics plc 2016 Long-Term Incentive Plan (the "**LTIP**") on 12 February 2016. Awards under the LTIP may be in the form of nil cost options or conditional share awards over Ordinary Shares, or the right to receive a cash amount (together, "**Awards**").

8.1.2 It is intended that Awards will be granted under the LTIP in the form of nil cost options shortly after Admission ("**Admission Awards**").

8.1.3 *Administration*. The LTIP is administered by the Remuneration Committee. The Remuneration Committee may determine the form, amount and other terms and conditions of Awards and determine the persons to whom Awards will be granted.

8.1.4 *Eligibility for Participation*. Employees, including the Executive Directors, of the Group will be eligible to participate in the LTIP at the discretion of the Remuneration Committee. It is intended that participation will be limited to Executive Directors and senior management.

8.1.5 *Grant of Awards*. With the exception of Admission Awards (as defined above), Awards may subsequently be granted within the period of 42 days following the day of announcement of the Company's results for any period; or at any other time as the Remuneration Committee may determine in exceptional circumstances, providing that Awards may not be granted during a close period. Awards granted under the LTIP will be granted by deed ("**Award Deed**") and evidenced with Award certificates, which will set out any additional terms, conditions, limitations and/or restrictions covering the Award, including, without limitation, any performance conditions (the "**Performance Conditions**").

8.1.6 *Nil cost options*. The Remuneration Committee may grant rights to any eligible employee in the form of options to acquire Ordinary Shares for a nil (or in the case of new issue shares, nominal) exercise price.

8.1.7 *Conditional Share Awards*. The Remuneration Committee may grant an Award to any eligible employee in the form of a right to receive Ordinary Shares without payment.

8.1.8 *Right to receive cash amount*. The Remuneration Committee may grant Awards on terms that may be satisfied by the payment of a cash sum equal to the market value of the notional number of Ordinary Shares in respect of which the Award vests.

8.1.9 *Performance Conditions*. The Remuneration Committee may, in its absolute discretion, grant Awards subject to the attainment of Performance Conditions stated at the date of grant. Any Performance Condition may be amended or substituted if one or more events occur which cause the Remuneration Committee to consider that an amended or substituted Performance Condition would be more appropriate. Any amended or substituted Performance Condition would not be materially less difficult to satisfy.

It is intended that the Performance Conditions for the Admission Awards will be measured over a three-year period (the "**Performance Period**"), commencing on the date of Admission, and calculated by reference to the Company's compound annual growth rate ("**CAGR**"), based on the benchmark of the FTSE Small Cap (excluding investment trusts) at the beginning of the Performance Period. Awards will not vest or become exercisable unless the Company's CAGR is at least 11.7%.

To determine the Admission Award amount, the Company's CAGR will be calculated at the end of each year in the Performance Period. If CAGR of at least 11.7% is achieved in the relevant year, the Participant will become entitled to receive a third of the Award amount, and such amount will be 'locked in' and cannot be forfeited in subsequent years. Awards will not vest or become exercisable until after the end of the Performance Period.

The Performance Period for subsequent Awards will commence at the beginning of the relevant financial year. It is intended that, initially, Performance Conditions for subsequent Awards will be calculated in the same manner as Admission Awards, save that if CAGR of at least 11.7 per cent. is achieved in the relevant year, the Participant will become entitled to receive a third of the base Award amount. For every 1% of additional CAGR achieved, the Award amount will increase incrementally, up to a cap of 21.7% CAGR, resulting in the maximum Award amount.

The Remuneration Committee will review and set appropriate Performance Conditions for future Awards, taking into account institutional investor guidelines and prevailing market practice.

8.1.10 *Holding Period.* An Award may be granted subject to a holding period, during which Ordinary Shares acquired by the participant pursuant to such Award cannot be sold. The holding period will begin on the vesting date (or, in the case of nil cost options, on the date on which the option is exercised) and end on such anniversary of the date of grant as the Remuneration Committee specifies.

8.1.11 *Individual limits*. Awards may not normally be granted to a participant over Ordinary Shares having a market value at the date of grant in excess of 1.25 times the individual's annual base salary. It is intended that the Admission Awards will be granted over Ordinary Shares having a market value at the date of grant of twice the relevant individual's pre-Admission annual base salary.

8.1.12 *Dividend equivalents*. The Remuneration Committee may grant an Award on the basis that it carries a right to receive a cash payment equal in value to ordinary dividends ("**Dividend Equivalent**") which would have been paid on vested Ordinary Shares during the period starting on the date of grant or, if the Award is subject to Performance Conditions, starting on the first day of the relevant performance period, and ending on the vesting date (or, if the Award is a nil cost option, on the day before the date on which such option first becomes exercisable). The Dividend Equivalent will be calculated at the discretion of the Remuneration Committee, and does not represent an entitlement to actual dividends on the underlying Ordinary Shares. On vesting (or in the case of nil cost options, exercise) the Remuneration Committee may satisfy any entitlement to a Dividend Equivalent by making a cash payment or by issuing or transferring Ordinary Shares to an equivalent value.

8.1.13 *Exercise / Vesting of Awards.* Awards will become exercisable or vest (as applicable) in whole or in part (subject to any applicable Performance Conditions) on a vesting or exercise date(s). The vesting or exercise dates will be specified by the Remuneration

Committee at the date of grant, but Awards will not normally become exercisable or vest prior to the third anniversary of the grant date. Where Performance Conditions apply, Awards will only become exercisable or vest to the extent such conditions have been satisfied. Any cash sum payable in respect of an Award which is the right to receive a cash amount will be paid as soon as practicable after the date on which it vests. Where an Award has been exercised or has vested and Ordinary Shares have not yet been allotted or transferred to the participant, the Remuneration Committee may determine that, instead of allotting or transferring the Ordinary Shares to the participant, it shall pay him a cash amount equal to the value of the Ordinary Shares he would otherwise have received. A nil cost option will normally remain exercisable until the tenth anniversary of the date of grant.

8.1.14 *Reduction for malus and claw-back.* The Remuneration Committee may reduce the number of Ordinary Shares under an unvested Award ("**malus**") or require the participant to repay an amount to the Company in respect of the value of a vested Award ("**claw-back**") in any of the following circumstances: material misstatement of financial results; the Participant engaging in fraud, gross misconduct or conduct which has a materially detrimental effect on the Company's reputation or justifying the Participant's summary dismissal; assessment of a Performance Condition being based on an error, or inaccurate or misleading information or assumption; a material failure of risk management; serious reputational damage to the Company; or any other circumstances which the Remuneration Committee considers to be similar in nature or effect. In assessing the repayable amount, the Remuneration Committee may take into account any tax or social security contributions applicable to the Award.

8.1.15 *Cessation of employment.* If a participant ceases to be employed by the Group as a Good Leaver, his Awards will become exercisable or vest on the normal exercise or vesting date, subject to applicable Performance Conditions having been achieved over the full performance period, and such Awards will be pro-rated for that part of the performance period elapsed to the date of cessation. The Remuneration Committee will have the discretion to disapply time pro-rating and to bring forward exercise/vesting to the date of cessation of employment. In the case of a nil cost option, a Good Leaver will normally be able to exercise their option during the period of six months following cessation of employment (or 12 months where cessation of employment is by reason of death). A "**Good Leaver**" is a participant who ceases employment by reason of death; injury, ill-health or disability; redundancy; retirement; the participant's employing company ceasing to be a Group member; the participant's employment being transferred, as part of business transfer, to a person who is not a Group member or under the control of a Group member; or any other reason that the Remuneration Committee in its discretion determines. If a participant who is not a Good Leaver ceases to be employed by the Group, his unvested Awards will lapse on the date of such cessation, unless the Remuneration Committee in its absolute discretion determines that Good Leaver treatment will apply.

8.1.16 *Corporate events.* In the event of a change of control (whether by way of a takeover offer or a scheme of arrangement or compromise) or a voluntary winding-up of the Company, Awards will vest or become exercisable immediately, to the extent any Performance Conditions have been met on the date of change of control. Such Awards will be pro-rated for that part of the performance period as has elapsed to the date of change of control, unless the Remuneration Committee in its discretion determines to permit a higher number of Ordinary Shares to vest or become exercisable. In the event of an internal reorganisation, Awards may be replaced by equivalent awards over shares in a new holding company.

8.1.17 *Variation of share capital.* In the event of a variation of the Company's share capital (whether by way of capitalisation or rights issue or sub-division or consolidation of the Ordinary Shares or a share capital reduction), the number of Ordinary Shares subject to an Award may be adjusted by the Remuneration Committee.

8.1.18 *Terms of Awards.* Awards granted under the LTIP are non-transferable, other than to a participant's personal representatives on the death of a participant. Any attempt to transfer will result in lapse of the Award. Participation in the LTIP will not be a term of a participant's contract of employment, and Awards will not form part of a participant's pensionable earnings.

8.1.19 *Shareholder Rights.* Except as otherwise provided in the applicable Award Agreement, all Ordinary Shares allotted or transferred to a participant on the vesting of an Award or the exercise of an option, will rank equally with other Ordinary Shares then in issue (except in respect of rights arising prior to the date of vesting or exercise, as the case may be).

8.1.20 *Overall Limits.* In any ten year period, (i) the number of Ordinary Shares which may be issued in respect of Awards granted after Admission under the LTIP and under any other employees' share plan adopted by the Company may not exceed 10 per cent. of the issued ordinary share capital of the Company from time to time, and (ii) the number of Ordinary Shares which may be issued in respect of Awards granted after Admission under the LTIP and under any other discretionary employees' share plan adopted by the Company may not exceed 5 per cent. of the issued ordinary share capital of the Company from time to time. Ordinary Shares held in treasury will be treated as newly issued Ordinary Shares for the purpose of these limits for as long as guidelines published by institutional investors so recommend. Ordinary Shares purchased in the market will not count towards these limits. Ordinary Shares transferred or issued pursuant to Awards that vested or were exercised prior to Admission will not count towards these limits.

8.1.21 *Amendment.* The Remuneration Committee may amend the LTIP at any time, provided that the prior approval of the Company's Shareholders in general meeting will be required for amendments to the advantage of eligible employees or participants, and majority participants' consent will be required for amendments which would adversely affect their subsisting rights. However, any minor amendment to benefit the administration of the LTIP, to take into account legislative changes, or to obtain or maintain favourable tax treatment, exchange control or regulatory treatment may be made by the Remuneration Committee without Shareholder and/or participants' approval.

8.1.22 *Term.* The LTIP will terminate 10 years from its adoption date unless the Board resolves to terminate it earlier. No Award may be granted more than 10 years after the LTIP is adopted. Awards granted before that date shall remain valid in accordance with their terms and the terms of the LTIP.

8.2 The Shield Therapeutics plc Company Share Option Plan

8.2.1 The Company adopted The Shield Therapeutics plc Company Share Option Plan (the "**CSOP**") on 12 February 2016. The CSOP is intended to satisfy the requirements of Schedule 4 of the UK Income Tax (Earnings and Pensions) Act 2003 for a tax qualified company share option plan. This will enable options granted under the CSOP potentially to benefit from favourable UK tax treatment ("**CSOP Options**"). The CSOP will also provide for the grant of non-tax advantaged options under an unapproved appendix ("**Non-CSOP Options**", and together with CSOP Options, "**Options**").

8.2.2 *Administration*. The CSOP is administered by the Remuneration Committee. The Remuneration Committee may determine the number of Ordinary Shares subject to an Option and other terms and conditions of Options and determine the persons to whom Options will be granted.

8.2.3 *Eligibility for Participation*. All employees of the Group will be eligible to participate in the CSOP, subject to limited exceptions to comply with legislative requirements. The Company does not intend to grant Options to Executive Directors.

8.2.4 *Grant of Options*. The current intention is that the grant of Options will be based on the achievement of performance conditions measured over the preceding financial year of the Company. Options may normally be granted within the period of 42 days following the day of announcement of the Company's results for any period; or at any other time as the Remuneration Committee may determine in exceptional

circumstances, providing that Options may not be granted during a close period. Options granted under the CSOP will be granted by deed (''**Option Deed**'') and evidenced with Option certificates, which will set out any additional terms, conditions, limitations and/or restrictions covering the Option, including, without limitation, terms as determined by the Remuneration Committee providing for the date or dates at which all, or specified tranches of, the Option will vest (the ''**Vesting Conditions**''), and any performance conditions to apply (the ''**Performance Conditions**'').

8.2.5 The Options will be granted at an exercise price equal to the market value of an Ordinary Share at the date of grant.

8.2.6 *Individual limits*. CSOP Options may be granted over Ordinary Shares with market value up to a maximum of £30,000 (calculated on date of grant). Options may not normally be granted to a participant over Ordinary Shares having a market value at the date of grant in excess of 1.25 times the individual's annual base salary.

8.2.7 *Performance Conditions*. The Remuneration Committee may, in its absolute discretion, grant Awards subject to Vesting Conditions, or the attainment of Performance Conditions, stated at the date of grant, although it does not currently intend to do so. Any Performance Condition may be amended or substituted if one or more events occur which cause the Remuneration Committee to consider that an amended or substituted Performance Condition would be more appropriate. Any amended or substituted Performance Condition would not be materially less difficult to satisfy.

8.2.8 *Exercise of Options.* Options will become exercisable in whole or in part (subject to any applicable Performance Conditions) on an exercise date(s), in accordance with the Vesting Conditions (if any). The exercise date(s) will be specified by the Remuneration Committee at the date of grant, and Options will normally become exercisable from the third anniversary of the grant date. Where Performance Conditions apply, Options will only become exercisable to the extent such conditions have been satisfied. Options may be satisfied by Ordinary Shares that are newly issued shares, held in treasury, or purchased in the market.

8.2.9 *Cessation of employment.* If a participant ceases to be employed by the Group as a Good Leaver, his Options may generally be exercised within 6 months of cessation of employment (or one year from his death), even if this occurs prior to the third anniversary of the date of grant (subject to Performance or Vesting Conditions, if any). A ''**Good Leaver**'' is a participant who ceases employment by reason of death; injury, ill-health or disability; redundancy; retirement; the participant's employing company ceasing to be a Group member; the participant's employment being transferred, as part of a business transfer, to a person who is not a Group member or under the control of a Group member; or any other reason that the Remuneration Committee in its discretion determines. If a participant who is not a Good Leaver ceases to be employed by the Group, his Options will lapse on the date of such cessation, unless the Remuneration Committee in its absolute discretion determines that the Good Leaver treatment will apply.

8.2.10 *Corporate events.* In the event of a change of control (whether by way of a takeover offer or a scheme of arrangement or compromise) or a voluntary winding-up of the Company, Options will be exercisable for a period of six months following such change of control, to the extent any Performance or Vesting Conditions have been met on the date of change of control. If a change of control causes CSOP Options to cease to qualify as such, they may be exercised during the period of 20 days before or after such change of control. In the event of an internal reorganisation, Options may be replaced by equivalent options over shares in a new holding company.

8.2.11 *Variation of share capital.* In the event of a variation of the Company's share capital (whether by way of capitalisation or rights issue or sub-division or consolidation of the Ordinary Shares or a share capital reduction), the number of Ordinary Shares subject to an Option may be adjusted by the Remuneration Committee in compliance with the relevant legislation.

8.2.12 *Terms of Options.* Options granted under the CSOP are non-transferable, other than to a participant's personal representatives on the death of a participant. Any attempt to transfer will result in lapse of the Options. Participation in the CSOP will not be a term of a participant's contract of employment, and Options will not form part of a participant's pensionable earnings.

8.2.13 *Shareholder Rights.* All Ordinary Shares allotted or transferred to a participant on the exercise of an Option will rank equally with other Ordinary Shares then in issue (except in respect of rights arising prior to the date of exercise).

8.2.14 *Overall Limits.* In any ten year period, the number of Ordinary Shares which may be issued in respect of Options granted after Admission under the CSOP and under any other employees' share plan adopted by the Company may not exceed 10 per cent. of the issued ordinary share capital of the Company from time to time. Ordinary Shares held in treasury will be treated as newly issued Ordinary Shares for the purpose of this limit for as long as guidelines published by institutional investors so recommend. Ordinary Shares purchased in the market will not count towards this limit. Ordinary Shares transferred or issued pursuant to Options that were exercised prior to Admission will not count towards this limit.

8.2.15 *Amendment.* The Remuneration Committee may not make any amendment to a key feature of the CSOP that would cause CSOP Options to cease to qualify as such. Otherwise, the Remuneration Committee may amend the CSOP at any time, provided that the prior approval of the Company's Shareholders in general meeting will be required for amendments to the advantage of eligible employees or participants, and the consent of a majority of participants will be required for amendments which would adversely affect their subsisting rights. However, any minor amendment to benefit the administration of the CSOP, to take into account legislative changes, or to obtain or maintain favourable tax treatment, exchange control or regulatory treatment may be made by the Remuneration Committee without Shareholder and/or participants' approval.

8.2.16 *Term.* The CSOP will terminate 10 years from its adoption date unless the Board resolves to terminate it earlier. No Option may be granted more than 10 years after the CSOP was adopted. Options granted before that date shall remain valid in accordance with their terms and the terms of the CSOP.

8.3 Employee Benefit Trust

At its discretion, the Company may establish an Employee Benefit Trust ("**EBT**") which would be able to acquire Ordinary Shares, either by purchase in the market or by way of subscription, to satisfy share or share option awards granted pursuant to the LTIP and/or the CSOP and/or such other share incentive arrangements as the Company may operate from time to time. The EBT would not, without prior Shareholder approval, acquire Ordinary Shares which would cause its holding to exceed 5 per cent. of the Ordinary Shares in issue from time to time. The EBT would be non-UK resident and would be funded by way of loans and/or other contributions from the Group to enable it to acquire Ordinary Shares.

8.4 Awards following Admission

As noted above, it is intended that the Company will grant Awards under the LTIP to Executive Directors and senior management, shortly after Admission. It is intended that such Awards will be granted over Ordinary Shares having a market value at the date of grant of twice the relevant individual's pre-Admission annual base salary. It is not intended that the Company will grant Options under the CSOP on or shortly after Admission.

8.5 Future remuneration policy

8.5.1 In anticipation of Admission, the Company undertook a review of its remuneration policy for Directors in order to ensure that it is appropriate for the listed company environment. In undertaking this review, the Company sought independent, specialist advice.

8.5.2 The Company's remuneration package for Executive Directors has been designed based on the following key principles:

(a) to promote the long-term success of the Company;

(b) to provide appropriate alignment with investors' expectations in relation to the Company's strategy and outcomes; and

(c) to provide a competitive package of base salary and benefits and short and long term incentives, with an appropriate proportion being subject to the achievement of stretching individual and corporate performance conditions.

8.5.3 In connection with these key principles, the Remuneration Committee has adopted new share plans. These are the LTIP and the CSOP (both summarised above). It is intended that Admission Awards will be granted under the LTIP over Ordinary Shares having a market value at the date of grant of twice the relevant individual's pre-Admission annual base salary. It is not intended that the Company will grant Options under the CSOP on or shortly after Admission.

8.5.4 In connection with these key principles, the Remuneration Committee has adopted an Annual Bonus Plan (the "**ABP**") which will apply from the financial year beginning 1 January 2016. The ABP provides for payment of discretionary annual performance-based bonuses to employees and executive directors of the Company and the Group ("**Bonuses**"). The ABP will be operated in line with the remuneration policy approved by Shareholders from time to time. The maximum potential bonus which may be awarded to a participant in respect of the relevant bonus year shall not exceed 100 per cent. of the participant's annual base salary. It is anticipated that Executive Directors may be awarded Bonuses which range between 60-100% of their annual base salary, and more junior employees may be awarded bonuses which range between 30-50 per cent. of their annual base salary. It is proposed that initially 50 per cent. of the Bonuses will be paid in cash and the remaining 50% be applied in the purchase of Ordinary Shares on an after tax basis in the market. Such Ordinary Shares will be subject to a 3-year retention period, and cannot be sold during that period. The Remuneration Committee will set performance targets for annual Bonuses at the start of each financial year, based on a combination of an individual's personal, departmental and Group performance.

8.5.5 Executive Directors' fixed and variable remuneration packages applying post-Admission have been determined taking into account:

(a) the role and experience of the Executive Directors;

(b) remuneration arrangements at comparable UK listed companies; and

(c) best practice for UK AIM-listed companies.

8.5.6 With effect from Admission, the Company will operate share ownership guidelines under which Executive Directors must at all times hold Ordinary Shares with a value equal to twice their annual base salary.

9 Material contracts

Save as described below, the Company has not (i) entered into any material contracts (other than contracts in the ordinary course of business) within the two years immediately preceding the publication of this document; or (ii) entered into any contracts that contain provisions under which the Company has any obligation or entitlement that is material to the Company as at the date of this document.

9.1 MRC Licence

PTL entered into a licence agreement with the MRC, dated 22 December 2011 ("**MRC Licence**"). Pursuant to the MRC Licence, the MRC granted PTL exclusive, worldwide licences to develop, make, have made, use, sell, offer for sale and import products covered by the licensed patents. The licensed patents comprise: (i) a platform patent ("**patent family P001**"), which is exclusively licensed to PTL in the relevant fields of phosphate binding for the treatment of renal diseases and/or intravenous iron for the treatment of iron deficiency anaemias (the "**Fields of Use**") and (ii) an application-specific patent relating to a ferric iron complex for use in the treatment of hyperphosphatemia ("**patent family P002**"), which is exclusively licensed to PTL without limitation as to field of use.

Under the MRC Licence, PTL is obligated to pay milestones of up to €10 million (€1 million of which has already been paid) upon the progression of PT20 into Phase 3 clinical trials, upon first application for marketing authorisation in any jurisdiction, and upon the grant of marketing authorisation in each of the EU, US and Japan. Royalties in respect of net sales of products are also payable. A high single digit royalty is payable on net sales of PT20. PTL is also obliged to pay between 10 and 40% of any net licensing revenues for any sub-licences granted in relation to the licensed patent rights, depending upon the stage of development at which the sub-license is granted.

PTL's royalty obligations are triggered upon PTL's (or any subsidiary or holding company of PTL) first commercial sale of the relevant product in a particular territory.

The MRC assumes primary responsibility for managing the filing, prosecution and maintenance of the licensed patent rights although it must consult with PTL (and PTL monitors the patents via its external patent attorneys). PTL pays 50 per cent. of the MRC's costs incurred in the filing, prosecution and maintenance of patent family P001 whilst PTL remains the only licensee (as the MRC is permitted to license this patent family outside of the fields of use relevant to PTL). PTL pays 100 per cent. of the MRC's costs incurred in the filing, prosecution and maintenance of patent family P002 (as this patent family is exclusively licensed to PTL without limitation as to field of use). The MRC must inform PTL if it decides not to prosecute or maintain any of the applications or granted patents in either patent family and PTL may take over the prosecution/maintenance of such applications/patents (provided that if patent family P001 has by then been licensed outside of the fields of use relevant to PTL, the best way forward in relation to that patent family must be discussed in good faith with the other licensee(s)).

Unless terminated earlier, the MRC Licence continues in force until the last of the licensed patent rights have expired or after ten years from the first commercial sale of any product, whichever is later.

The MRC may terminate the agreement by notice to PTL if:

(a) PTL challenges the secret or substantial nature of the licensed know-how or the validity of the licensed patent rights;

(b) PTL commits and fails to remedy a material breach of the MRC Licence within 30 days; or

(c) PTL suffers an insolvency event.

9.2 AOP Pharma Distribution Agreement

ITH entered into an exclusive distribution agreement with IRORPH, dated 27 October 2010 ("**Distribution Agreement**"), as amended on 12 February 2016. Pursuant to the terms of the Distribution Agreement, ITH appointed IRORPH as its exclusive distributor to distribute Feraccru in the following countries: Albania, Austria, Bosnia, Bulgaria, Croatia, Czech Republic, Egypt, Former Yugoslav Republic of Macedonia, Hungary, Jordan, Poland, Romania, Russia, Saudi Arabia, Serbia, Slovakia, Slovenia, Syria, Turkey, Ukraine, United Arab Emirates (together, the "**Territory**").

ITH also granted IRORPH the sole right in the Territory to use trade marks approved by ITH from time to time, in relation to the sale of Feraccru.

IRORPH transferred all of its rights and obligations under the Distribution Agreement to AOP Pharma pursuant to a novation agreement between ITH, IRORPH and AOP Pharma dated 19 January 2015.

AOP Pharma is obliged to purchase Feraccru only from ITH and is prohibited from distributing or manufacturing any goods which compete with Feraccru, inside and outside of the Territory, from the Commencement Date (as defined below). The purchase price of Feraccru is agreed to be a double digit percentage over the ex factory price with the percentage being based upon a basket of pharmaceutical list prices for Feraccru in the Territory and being revised annually.

Given the exclusive nature of the Distribution Agreement, ITH agreed that it would not itself supply Feraccru to approved customers in the Territory and that it would, to the extent permitted by law, restrict other distributors to which it sells Feraccru from making active sales

to approved customers in the Territory. However, ITH has the right to appoint other distributors for the marketing, promotion and sale of Feraccru in any territory during the 90 day period prior to the expiry or termination of the Distribution Agreement.

The Distribution Agreement has an initial five-year term, which commences on the date when Feraccru is first granted marketing authorisation in a country in the Territory (the "Commencement Date"), unless terminated earlier. The Distribution Agreement grants AOP Pharma an option to renew on the same terms and conditions for another three periods of 5 years, such option to be exercised at least 12 months prior to the expiry of the Distribution Agreement.

If the Company wishes to enter into negotiations with any third party in respect of the distribution of Feraccru in Denmark, Sweden, Norway and Finland, AOP Pharma shall have the right to match the terms of distribution on offer from that third party.

Either party may give notice in writing to the other terminating the Distribution Agreement if, *inter alia*, (i) the other party fails to pay any amount due under the Distribution Agreement and remains in default for not less than 14 days after being notified to make such payment; (ii) the other party commits a material breach of the Distribution Agreement and fails to remedy the breach within 4 days of being notified in writing to do so; (iii) the other party suffers an insolvency event; (iv) the other party ceases, or threatens to cease, to carry on its business; or (v) the other party purports to assign its rights or obligations under the Distribution Agreement other than in accordance with the Distribution Agreement.

9.3 Vitra APA

The Group acquired certain intellectual property related to Feraccru from Vitra Pharmaceuticals, pursuant to an asset purchase agreement dated 23 February 2010 (the "**Vitra APA**"). Under the Vitra APA, Vitra Pharmaceuticals has the right to receive a mid-single digit royalty in respect of products falling within the scope of the acquired intellectual property. On 12 February 2016, ITH entered into an agreement with Vitra Pharmaceuticals which, subject to Admission, amended certain clauses of the Vitra APA in order to cancel Vitra Pharmaceuticals' rights to the reversion of the acquired intellectural property. In return, ITH agreed, subject to Admission to pay a lump sum of £250,000 (guaranteed by the Company) to Vitra Pharmaceuticals.

9.4 Initial Framework Agreement

SHG, ITH, PTL, W.Health, IRORPH, Carl Sterritt, Richard Jones and others entered into a framework agreement dated 18 September 2015 (the "**Initial Framework Agreement**") which provided *inter alia* for the entry into the share exchange agreement described in paragraph 9.6 below and the agreement for the acquisition by the Company of SHG described in paragraph 9.7 below. This agreement was terminated by the parties on 12 February 2016 and replaced by the Corporate Reorganisation Framework Agreement described in paragraph 9.5 below.

9.5 Corporate Reorganisation Framework Agreement

On 12 February 2016, the Company, SHG, ITH, PTL, W. Health, IRORPH, Carl Sterritt, Richard Jones and others entered into a framework agreement pursuant to which the parties agreed to effect the outstanding elements of the Corporate Reorganisation (the "**Corporate Reorganisation Framework Agreement**"). This agreement provided *inter alia* for the entry into the W.Health Replacement Option and the share exchange agreement referred to in paragraphs 9.8 and 9.10 below.

9.6 Share exchange agreement relating to the acquisition by SHG of a minority stake in ITH

On 18 September 2015, SHG and IRORPH entered into a contribution in kind agreement pursuant to which SHG agreed to acquire 9,987,760 preferred shares in ITH and 1,361,290 common shares in ITH from IRORPH, together constituting 18.3 per cent. of the issued share capital of ITH, in return for the issue of 23,964,383 shares in SHG, constituting 20.8 per cent. of the then issued share capital of SHG.

9.7 Share exchange agreement relating to the acquisition by the Company of SHG

On 1 October 2015, W.Health, IRORPH, Carl Sterritt, Christian Schweiger and all of the other shareholders of SHG entered into a share exchange agreement with the Company pursuant to which the Company agreed to acquire the entire issued share capital of SHG in return for the issue of shares in the Company in the same proportions and in the same classes as those then held by such transferring shareholders in SHG.

9.8 W. Health Replacement Option

On 12 February 2016, W. Health and the Company entered into an option agreement pursuant to which W. Health was granted an option to subscribe for 19,844,447 Ordinary Shares for an aggregate subscription price of €4,981,703. This option was granted by the Company in consideration of the release of W. Health's options in SHG and W. Health agreeing to the transfer of its preference shares in the Company (as part of the Corporate Reorganisation) and in release of a preference amount payable by SHG to W. Health as a result of the Corporate Reorganisation and Admission.

9.9 IRORPH Top-up Option

On 12 February 2016, IRORPH and the Company entered into an option agreement pursuant to which IRORPH was granted an option to subscribe for 742,456 Ordinary Shares at a price of 1.5p per Ordinary Share. This option was granted as part of the Corporate Reorganisation.

9.10 Share exchange agreement relating to the acquisition by the Company of PTL

On 12 February 2016, W.Health, Carl Sterritt, Richard Jones and all of the other shareholders of PTL entered into a share exchange agreement with the Company pursuant to which the Company agreed to acquire the entire issued and to be issued share capital of PTL (including certain shares to be issued prior to Admission pursuant to the exercise of options) in return for the issue of 19,887,791 New Shares. This agreement is conditional upon Admission and the transfer of shares in PTL pursuant to this agreement will take effect upon Admission.

9.11 PTL Subscription Agreements

On 4 September 2015, PTL entered into subscription agreements with each of Colin Baker, Andrew Heath, Carre Rouge Ltd, Tony Wan, Martin Haigh, Karen Menzies, Nick Hawkins, Eva Maria Widhalm and Clive Harris (the "**Subscribers**") whereby the Subscribers applied for the allotment and issue to them of new series B shares in PTL. The subscription for 68,036 new series B shares completed, on 4 September 2015, raising an aggregate of £900,000.

9.12 Lock-up Agreements

Each of Carl Sterritt, Richard Jones, Andrew Heath, Christian Schweiger, W. Health and IRORPH have entered into Lock-up Agreements with the Company dated 12 February 2016 pursuant to which they have agreed to be subject to a twelve month lock-up period, during which time, subject to certain exceptions, they may not issue, offer, sell or contract to sell, or otherwise dispose of any Ordinary Shares, Warrants, and any Ordinary Shares that may be issued pursuant to the exercise of Warrants, or enter into any transaction with the same economic effect as the foregoing (each a "**Disposal**"). In addition, they have also agreed that any Disposal in the subsequent six month period will be undertaken by Liberum (for so long as Liberum remains the Company's nominated adviser and broker) from time to time.

9.13 Placing Agreement

The Company entered into the Placing Agreement on 12 February 2016, further details of which are set out in paragraph 13.1 below.

9.14 Subscription Agreements

On 12 February 2016, certain existing Shareholders and other investors have entered into the Subscription Agreements. Further details are set out in paragraph 13.2 below.

9.15 Warrant Instrument

On 12 February 2016 the Company executed a Warrant instrument by way of a deed poll creating the Warrants. Particulars of the Warrants are set out in Part 9 (*Particulars of the Warrants*).

9.16 Engagement Letter and Nominated Adviser and Broker Agreement with Liberum

An engagement letter dated 27 November 2015 between (1) the Company and (2) Liberum pursuant to which the Company *inter alia* appointed Liberum to act as nominated adviser and sole bookrunner to the Company in connection with Admission and the Placing and as nominated adviser and broker following Admission.

In connection with its role as nominated adviser and broker following Admission, the Company has agreed to pay to Liberum a fee of £60,000 (plus VAT) in the first year of appointment, £70,000 (plus VAT) in the second year of appointment and £80,000 (plus VAT) in the third year of appointment and per annum thereafter. Liberum's appointment as nominated adviser and broker commenced on the date of the letter and may be terminated by either party giving the other three months' written notice.

10 Properties, Investments and Assets

The following are the principal establishments of the Group:

Name and location	Type of facility/ Investment	Tenure
Studio 6, Third Floor, Northern Design Centre, Abbotts Hill, Baltic Business Quarter, Gateshead, Tyne and Wear NE8 3DF	Office	Leasehold
3-8 Bolsover Street, London, W1W 6AB	Office	Office Service Agreement

11 UK Taxation

11.1 General

The following statements are intended to apply only as a general guide to certain UK tax considerations, and are based on current UK tax law and current published practice of HM Revenue and Customs ("**HMRC**"), both of which are subject to change at any time, possibly with retrospective effect.

The statements relate only to certain limited aspects of the UK taxation treatment of shareholders and warrantholders who are resident and, in the case of individuals, domiciled in (and only in) the United Kingdom for UK tax purposes (except to the extent that the position of non-UK resident shareholders is expressly referred to), who hold the Ordinary Shares or Warrants as investments (other than under an individual savings account or a self-invested personal pension) and who are the beneficial owners of both the Ordinary Shares (and any dividends paid on them) and Warrants.

The statements may not apply to certain classes of shareholders or warrantholders such as (but not limited to) persons acquiring their Ordinary Shares or Warrants in connection with an office or employment, dealers in securities, insurance companies, collective investment schemes, persons who own more than 10 per cent. of the Ordinary Shares or Warrants or persons making or holding their investment in the Ordinary Shares or Warrants with the purpose of obtaining a UK tax advantage.

Prospective subscribers for, or purchasers of, Ordinary Shares or Warrants who are in any doubt as to their tax position regarding the acquisition, ownership and disposition of the Ordinary Shares or Warrants or who are subject to tax in a jurisdiction other than the United Kingdom are strongly recommended to consult their own tax advisers.

11.2 Dividends

The Company will not be required to withhold tax at source from dividend payments it makes.

11.2.1 UK resident individual shareholders

An individual shareholder who is resident in the United Kingdom for tax purposes and who receives a dividend from the Company will be entitled to a tax credit which may be set off against his total income tax liability on the dividend. Such an individual shareholder's liability to income tax is calculated on the aggregate of the dividend and the tax credit (the gross dividend) which will be regarded as the top slice of the individual's income. The tax credit will be equal to 10 per cent. of the gross dividend (i.e. the tax credit will be one-ninth of the amount of the dividend). A UK resident individual shareholder who is not liable to income tax in respect of the gross dividend will not be entitled to reclaim any part of the tax credit. An individual shareholder who is resident in the United Kingdom for tax purposes and who receives a dividend from the Company will, subject to any reliefs or allowances available to that shareholder, be subject to income tax on that dividend.

For the 2016/2017 tax year (commencing 6 April 2016) and for subsequent tax years, the 10% dividend tax credit will no longer be available. Instead, there is to be a new dividend tax allowance and individuals will pay no income tax on dividend income (from any source) that is covered by the allowance. The amount of the allowance and rates of income tax on dividend income above the allowance for the tax year 2016/2017 are:

Dividend allowance	£5,000
Dividends taxed in the basic rate band	7.5%
Basic Rate band	*£0-£32,000**
Dividends taxed in the higher rate band	32.5%
Higher Rate band	*£32,001 – £150,000**
Dividends taxed in the additional rate band	38.1%
Higher rate band	*£150,001 and over**

*(subject to other reliefs and allowances, including the personal allowance)

11.2.2 Companies

A shareholder within the charge to United Kingdom corporation tax will generally be exempt from UK corporation tax on any dividend received from the Company so long as the dividends fall within an exempt class and certain conditions are met.

11.2.3 UK resident exempt shareholders

UK resident shareholders who are not liable to UK taxation on dividends, including pension funds and charities, will not be entitled to reclaim any tax credit attaching to any dividend paid by the Company.

11.2.4 Non-UK resident shareholders

A shareholder resident outside the United Kingdom for tax purposes will not generally be able to claim repayment from HMRC of any part of any tax credit attaching to a dividend received from the Company, although this will depend on the existence and terms of any double taxation convention between the UK and the country in which such shareholder is resident.

A non-UK resident shareholder may also be subject to taxation on dividend income under local law. A shareholder who is not solely resident in the United Kingdom for tax purposes should consult his own tax advisers concerning his tax liabilities (in the United Kingdom and any other country) on dividends received from the Company.

11.3 Capital Gains

A disposal or deemed disposal of Ordinary Shares or Warrants by a shareholder or warrantholder who is resident in the United Kingdom for tax purposes may, depending on the shareholder's circumstances and subject to any available exemptions and reliefs (such as the annual exempt amount for individuals and indexation allowance for corporate shareholders), give rise to a chargeable gain or an allowable loss for the purposes of UK taxation of capital gains.

An individual shareholder or warrantholder who has ceased to be resident in the United Kingdom for tax purposes for a period of less than five years and who disposes of Ordinary Shares or Warrants during that period may also be liable on his return to the United Kingdom to UK taxation on any capital gain realised (subject to any available exemption or relief).

If an individual shareholder or warrantholder who is subject to income tax at either the higher or the additional rate becomes liable to UK capital gains tax on the disposal of Ordinary Shares or Warrants, the applicable rate will be 28 per cent. For an individual shareholder or warrantholder who is subject to income tax at the basic rate and liable to UK capital gains tax on such disposal, the applicable rate would be 18 per cent.

11.4 Stamp duty and stamp duty reserve tax

No UK stamp duty will be payable on the issue by the Company of Ordinary Shares. For as long as Ordinary Shares and Warrants are admitted to trading on AIM on issue (and not listed on a recognised stock exchange), their transfer will be exempt from stamp duty and agreements for their transfer will be exempt from SDRT. Otherwise, transfers of Ordinary Shares and Warrants for value will generally give rise to a liability to pay UK *ad valorem* stamp duty, or stamp duty reserve tax, at the rate of 0.5 per cent. of the amount or value of the consideration (rounded up in the case of stamp duty to the nearest £5).

11.5 Inheritance Tax

The Ordinary Shares and Warrants will be assets situated in the United Kingdom for the purposes of UK inheritance tax. However, a holding of unquoted shares in an unquoted company can be eligible for 100 per cent. business property relief from inheritance tax provided that the business of the company does not consist wholly or mainly of dealing in stocks or shares, land or buildings or the making or holding of investments, that the investor holds the shares for the relevant qualifying period (normally two years) and other conditions for relief are satisfied.

The Company will be unquoted for these purposes for so long as its shares are admitted to trading on AIM but are not listed on any recognised stock exchange.

Shareholders of Ordinary Shares and warrantholders of Warrants should consult an appropriate tax advisor as to any inheritance tax implications if they intend to make a gift or transfer of Ordinary Shares or Warrants at less than market value or envisage that the Ordinary Shares or Warrants may form part of their estate on death.

12 The proposed financial transaction tax (''FTT'')

The European Commission proposal for a common FTT continues to be considered by Belgium, Germany, Greece, Spain, France, Italy, Austria, Portugal, Slovenia and Slovakia (the ''**participating Member States**'') and a start date in June 2016 has been suggested. The proposed FTT has very broad scope and whether it might apply to certain dealings in the Ordinary Shares and Warrants (including secondary market transactions) in certain circumstances remains unclear. Prospective holders of the Ordinary Shares and Warrants are advised to seek their own professional advice in relation to the FTT.

13 Placing Arrangements

The Company, the Directors and Liberum entered into the Placing Agreement on 12 February 2016, pursuant to which:

13.1.1 on the terms and subject in each case to certain conditions as are customary in an agreement of this nature (the last condition being Admission) contained in the Placing Agreement and described below, the Company has agreed to allot and issue, at the Placing Price, the 20,226,665 New Shares and 10,891,277 Warrants to be issued in connection with the Institutional Placing.

13.1.2 Liberum has agreed to procure subscribers for such New Shares and Warrants to be issued by the Company pursuant to the Placing Agreement;

13.1.3 in consideration for their services and subject to Admission occurring:

(a) the Company shall pay to Liberum:

(i) a corporate finance fee of £150,000; and

(ii) a commission of 3.2 per cent. of the aggregate value at the Placing Price of the Placing Shares placed to placees pursuant to the Institutional Placing who are not existing shareholders); and

(iii) a commission of up to £400,000 in proportion to the number of warrants exercised;

13.1.4 the Company's obligation to issue new Placing Shares and Warrants under the Placing Agreement is, and the several obligations of Liberum to procure subscribers for Placing Shares are, subject to certain conditions that are customary for an agreement of this nature. These conditions include, amongst others, the absence of any breach of warranty under the Placing Agreement, Admission occurring by no later than 8.00 a.m. on 26 February 2016 and the Subscription Agreements and the Reorganisation Agreements having been entered into and duly completed in all material respects (save as regards Admission) and continuing to be enforceable against each of the parties thereto (subject to Admission). In addition, Liberum has the right to terminate the Placing Agreement prior to Admission in certain specified circumstances that are customary in an agreement of this nature;

13.1.5 the Company has agreed to pay the costs, charges, fees and expenses of the Placing (together with any related value added tax);

13.1.6 the Company and the Directors have each given customary representations, warranties and undertakings to Liberum, and the Company has given customary indemnities to Liberum. The liability of the Company under the Placing Agreement is not limited as to time or amount; and

13.1.7 the Company has agreed not to issue, offer, sell, issue options in respect of, contract to sell or otherwise dispose of, directly or indirectly, any Ordinary Shares or any securities of the Company (or any interest therein or in respect thereof) that are substantially similar to the Ordinary Shares including, but not limited to, any securities that are convertible into or exchangeable for, Ordinary Shares or enter into any transaction with the same economic effect as any of the foregoing (other than Ordinary Shares issued pursuant to the exercise of Warrants or Ordinary Shares and options issued pursuant to the employee stock option plans existing on the date of this document) during the period beginning on the date of this document and ending on the date six months after Admission, without the prior written consent of Liberum.

13.2 IRORPH, Carl Sterritt, Christian Schweiger, Karen Nugent, Eva-Maria Widhalm and Stephenson Harwood LLP have entered into Subscription Agreements with the Company to subscribe for, in aggregate, 1,439,997 New Shares and 775,381 Warrants at the Placing Price. Pursuant to this subscription, Stephenson Harwood LLP has agreed to receive Placing Shares in satisfaction of £100,000 of their professional fees. Completion of the Subscription is conditional on Admission. The Subscription is irrevocable and each subscriber has given customary undertakings to the Company.

14 Litigation

There are no governmental, legal or arbitration proceedings, and the Company is not aware of any governmental, legal or arbitration proceedings pending or threatened, during the 12 months preceding the date of this document which may have, or have had in the recent past, a significant effect on the financial position or profitability of the Group.

15 Significant change

As at the date of this document, there has been no significant change in the financial or trading position of the Group since 30 June 2015, save for the acquisition of SHG by the Company described in paragraph 9.7 above, and other elements of the Corporate Reorganisation detailed in paragraph 2 of Part 10 (*Additional Information*) of this document and the equity fundraising in PTL detailed in paragraph 2.2 of Part 2 (*Information on the Company and the Group*).

16 Current trading and prospects

Since 30 June 2015, the Group has been progressing its plans in respect of the development of both Feraccru and PT20.

For Feraccru, the main focus has been to continue the interaction with the EMA with the aim of securing marketing authorisation during the first quarter of 2016, the associated preparation for commercial launch of Feraccru in Europe as well planning for the Phase 3 clinical study for patients who have CKD and IDA and starting the Phase 3b comparator study to IV iron. As a result the Group has continued to incur expenditure with respect to SHG in supporting the clinical trials and expects to increase the rate of expenditure for the remainder of 2016 financial year as the expected approval date for Feraccru gets closer and the preparation of both clinical trials intensifies and headcount is increased in advance of commercialisation. For PT20, following the completion of the Phase 2b pivotal study, the Company is currently reviewing the data and working towards a meeting with the FDA in 2016 and as such expenditure since 30 June 2015 has been at a lower run rate than the first six months and will continue to be for the forseable future.

Overall the Board of Shield view the remainder of 2016 with confidence.

17 Net proceeds and expenses

Through the issue of 21,666,662 New Shares pursuant to the Placing, the Company expects to raise gross proceeds of approximately £32.5 million. The aggregate expenses of, or incidental to, Admission and the Placing to be borne by the Company are estimated to be approximately £2.4 million, which the Company intends to pay out of the proceeds to the Placing.

The Company expects to receive net proceeds from the Placing of approximately £30.1 million.

In addition to the net proceeds of the Placing receivable by the Company, the Company will receive an additional £3.79 million upon Admission pursuant to the exercise of the W. Health Replacement Option.

If the Warrants are exercised in full, the Company will receive a further £17.5 million in gross proceeds.

18 Working capital

In the opinion of the Directors, having made due and careful enquiry, the working capital available to the Company and its Group will be sufficient for its present requirements, that is, for at least twelve months from the date of Admission.

19 General

19.1 Where information contained in this document has been sourced from third parties, the Company confirms that this information has been accurately reproduced and that, so far as the Company is aware and is able to ascertain from information published by that third party, no facts have been omitted which would render the reproduced information inaccurate or misleading.

19.2 Liberum has given and has not withdrawn its written consent to the publication of this document with the inclusion of its name and references to it in the form and context in which it appears.

19.3 The financial information contained in this document which relates to PTL does not constitute full statutory accounts as referred to in section 434 of the Companies Act. Statutory consolidated audited accounts of the Company, on which the auditors have given unqualified reports and which contained no statement under section 498(2) or (3) of the Companies Act, have been delivered to the Registrar of companies in respect of the three accounting periods ended 31 December 2014.

19.4 Save as otherwise disclosed in this document, and except for fees payable to the professional advisers named in this document or payments to trade suppliers, no person has received any fees, securities in the Company or other benefit to the value of £10,000 or more, whether directly or indirectly, from the Company within the 12 months preceding the application for Admission, or has entered into any contractual arrangement to receive from the Company, directly or indirectly, any such fees, securities or other benefit on or after Admission.

19.5 The Company has paid, or has entered into contractual arrangements to pay:

- £197,000 to Kellerhals Anwälte for legal advice in relation to Swiss law matters;
- £125,000 to Square One Law LLP for legal advice in relation to English law matters;

- £200,000 to Investec Bank plc and £150,000 to Canaccord Genuity Limited relating to financial advisory services;
- £21,000 to Nedbank for services in relation to the Group's previous employee incentive arrangements; and
- £12,000 to H2 Gelnfern for advice in relation to remuneration benchmarking.

20 Auditors

The auditors to the Company are KPMG LLP who is registered to carry on audit work by The Institute of Chartered Accountants in England and Wales ("**ICAEW**"). The firm is a member of the ICAEW Practice Assurance scheme and is subject to the jurisdiction of The Accountancy and Actuarial Discipline Board.

21 Reporting Accountant and Consent

KPMG LLP (a member of the ICAEW) has given and has not withdrawn its written consent to the inclusion in this document of its reports set out in Parts 5 (*Historical Financial Information for SHG*) and 6 (*Historical Financial Information for PTL)* of the document in the form and context in which they appear and has authorised the contents of those parts of the document which compose its reports for the purposes of the AIM Rules for Companies. As the Placing Shares have not been and will not be registered under the Securities Act, KPMG LLP has not filed and will not be required to file a consent under the Securities Act.

22 Market Report Providers and Consent

22.1 GfK is a leading consultancy specialising in the assessment of healthcare companies, projects, products and markets and assisting in their development. GfK has no material interest in the Company.

22.2 GfK has given and has not withdrawn its written consent to the inclusion in this document of its market report in Part 8 (*Market Report*) of this document in the form and context in which it appears and has authorised that part of the document which comprises its report for the purposes of the AIM Rules for Companies. As the Placing Shares have not been and will not be registered under the Securities Act, GfK has not filed and will not be required to file a consent under the Securities Act.

23 Patent Agent and Consent

23.1 Stratagem acts as intellectual property advisors and patent and trade mark attorneys to the Company. Stratagem has no material interest in the Company.

23.2 The professional staff at Stratagem who advise the Company are UK Chartered Patent Attorneys and European Patent Attorneys, and UK Registered Trade Mark Attorneys and European Trade Mark Attorneys, and possess the necessary technical specialism and are legally qualified to act for technology clients before the UK Intellectual Property Office, the European Patent Office and the International Patent and Trade Mark Office.

23.3 Stratagem has given and has not withdrawn its written consent to the inclusion in this document of its market report in Part 7 (*Patent Agent's Report*) of this document in the form and context in which it appears and has authorised that Part of the document which comprises its report for the purposes of the AIM Rules for Companies. As the Placing Shares have not been and will not be registered under the Securities Act, Stratagem has not filed and will not be required to file a consent under the Securities Act

Dated 12 February 2016