Pharmaceuticals & Biotechnology

Source: Eikon Thomson Reuters

Market data	
EPIC/TKR	**STX**
Price (p)	**94.7**
12m High (p)	100.0
12m Low (p)	23.0
Shares (m)	117.0
Mkt Cap (£m)	110.9
EV (£m)	101.1
Free Float*	32.5%
Market	AIM

**As defined by AIM Rule 26*

Description

Shield Therapeutics is a commercial-stage pharmaceutical company delivering innovative specialty pharmaceuticals that address patients' unmet medical needs, with an initial focus on anaemia associated with renal and gastrointestinal disorders.

Company information	
CEO	Carl Sterritt
CFO (Interim)	Tim Watts
Chairman	James Karis

+44 207 186 8500
www.shieldtherapeutics.com

Key shareholders	
Directors	8.9%
W. Health	48.1%
MaRu AG	10.8%
R. Griffiths	7.8%
C. Schweiger	4.8%
USS	4.4%

Diary	
Jun'19	AGM
27-Jul	Feraccru PDUFA date

Analysts

Martin Hall 020 7194 7632
mh@hardmanandco.com
Dorothea Hill 020 7194 7626
dmh@hardmanandco.com
Grégoire Pavé 020 7194 7628
gp@hardmanandco.com

SHIELD THERAPEUTICS

All in the execution

Shield Therapeutics (AIM: STX) is a commercial-stage pharmaceutical company delivering specialty products that address patients' unmet medical needs, with an initial focus on treating iron deficiency with Feraccru®. Following IPO and EU approval of Feraccru, both in February 2016, STX has made good progress with its clinical and commercial strategy, most recently demonstrating in a phase 3 trial that oral Feraccru is as effective as intravenous iron. Management has secured commercialisation agreements and is now awaiting an FDA decision in 3Q'19. The remaining risks lie in US approval and in successful execution of commercialisation.

- **Strategy:** STX's strategy is to out-license the commercial rights to its products to partners with marketing and distribution expertise in target markets. These agreements allow STX to retain its intellectual property (IP) and to continue to invest in its R&D pipeline, while benefiting from immediate and long-term value.

- **Feraccru:** A novel iron replacement therapy, Feraccru is approved across Europe for treatment of iron deficiency (ID) in adults with or without anaemia. ID results from depletion of iron stores, affecting production of red blood cells (which carry oxygen). Feraccru is well tolerated, having a similar side-effect profile to placebo.

- **Valuation:** DCF analysis with conservative assumptions generated a risk-adjusted valuation for Feraccru of £184m. This assumes successful commercialisation across Europe and the US in selected patient sub-segments with iron deficiency anaemia, to reach annual sales of $640m/£490m at peak.

- **Risks:** All drug companies carry development risk. However, STX has limited risk because of Feraccru's simplicity and clinical profile. Also, Feraccru has already received more than one regulatory approval and is generating sales. The main risks are commercial execution and the FDA decision on US approval.

- **Investment summary:** STX is at an exciting juncture. It has delivered on all goals set at the time of its IPO in 2016. Feraccru has been validated by regulatory approval and the commercial deals in Europe are likely to be repeated in the US. Given its advancement since IPO and its potential, STX's market capitalisation of £110.9m, significantly below the IPO value, makes for an interesting proposition.

Financial summary and valuation

Year-end Dec (£m)	2016	2017	2018	2019E	2020E
Gross revenues	**0.34**	**0.64**	**11.88**	**2.83**	**2.00**
Sales	0.30	0.64	0.86	0.63	2.00
R&D	-2.03	-4.71	-4.30	-4.73	-2.51
Other income	0.04	0.00	11.03	2.20	0.00
EBITDA	-10.29	-17.92	-1.80	-6.30	-6.45
Underlying EBIT	-10.47	-18.34	-2.25	-6.75	-6.90
Reported EBIT	-12.46	-20.95	-5.17	-9.67	-9.82
Underlying PBT	-10.43	-18.35	-2.24	-6.73	-6.93
Statutory PBT	-15.60	-20.99	-5.15	-9.65	-9.85
Underlying EPS (p)	-9.73	-15.08	0.96	-4.62	-5.60
Statutory EPS (p)	-14.84	-17.43	-1.54	-7.86	-8.03
Net (debt)/cash	20.98	13.30	9.78	6.02	0.83
Capital increase	33.51	11.88	0.00	0.00	0.00

Source: Hardman & Co Life Sciences Research

Table of contents

Executive summary

Investment summary

When STX listed on the AIM in February 2016, it raised £30.1m (net) of new capital at 150p a share, giving it a market capitalisation of £162m. This supported investment in the continued development of Feraccru and the initial phase of the product's commercial rollout. Although management has delivered on its strategy to complete clinical trials that would deliver EU and US regulatory approvals of Feraccru and has already achieved sales, STX's market capitalisation remains significantly below the IPO value.

The STX investment proposition is straightforward. Feraccru:

- is an EU-approved, simple, oral therapeutic containing iron, essential for normal body function, which addresses a clear unmet need in a highly prevalent disorder;
- is well understood scientifically with a good tolerability profile;
- readily fits into the treatment pathway consistent with normal clinical practice;
- and has a clear commercial strategy, validated by the Norgine partnership in the EU, which needs to be repeated in the US.

STX, meanwhile, has a balance sheet that supports modest cash burn until the second half of 2020, which is likely to be boosted by further R&D and sales milestones from Norgine and/or upfront payments from new commercial partners.

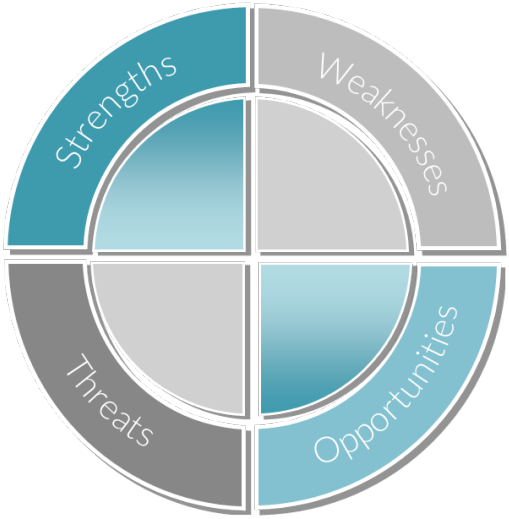
Valuation summary

DCF analysis with conservative assumptions generated a risk-adjusted valuation for Feraccru of £184.3m. This assumes successful commercialisation across Europe and the US in selected patients with iron deficiency anaemia to reach peak annual sales of $640m/£490m. Feraccru provides most of the group's value, which was £194.2m on a sum-of-parts basis, or £1.66/share.

SWOT analysis

- Feraccru tolerability profile exceeds that of existing oral therapies
- Capsules easy to administer; fit within normal clinical practice
- Feraccru mechanism easy to understand
- Feraccru already in sales

- Small player in a competitive environment
- Commercialisation deals take time to close
- Feraccru not yet approved in the US

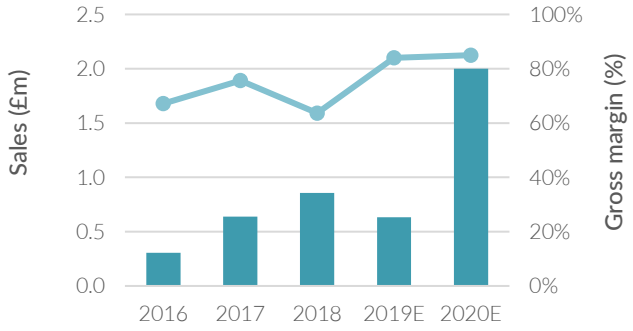


- Time and cost of additional clinical trials
- Competitive field; patent objections
- Time needed for successful execution of strategy
- Unfortunate, although resolved, complication with trial read-out in 2018

- Iron deficiency a very large unmet need
- Clear strategic opportunity in underserved patients
- Iron supplement market likely to grow
- Opportunity for a good deal in the US if Feraccru approved

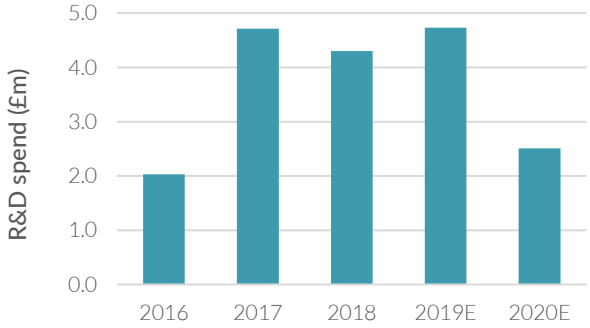
Source: Hardman & Co Life Sciences Research

Sales & gross margin



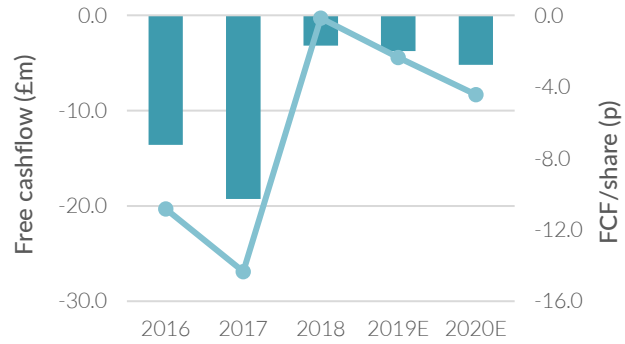
- Sales (the bars in the chart to the left) are expected to be driven entirely by Feraccru royalties from 2019
- Drop in 2019 sales reflects the transition from direct selling by STX to royalties from Norgine in 4Q'18
- Accelerated growth expected in 2020 due to launches in additional European countries and potentially the US (depending on the FDA's approval decision in July 2019)
- Gross margin (the line in the chart to the left) is stable in 2019/2020: COGS remain at ca.15%, but are likely to reduce once Feraccru launched in the US

R&D investment



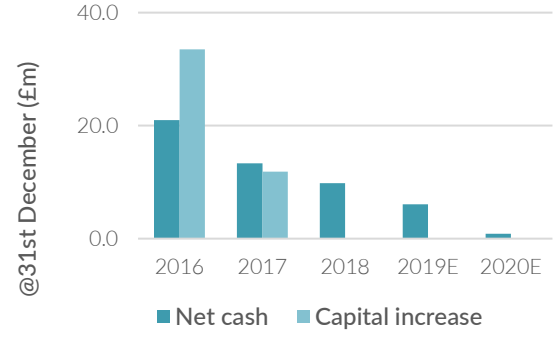
- R&D spend expected to increase in 2019 with the initiation of the large Feraccru Phase 3 paediatric study and to remain between £2m and £3m in 2020
- Spend in 2017 reflected investment in the AEGIS-CKD trial and in 2018 included AEGIS-H2H
- Future R&D investment timing is flexible on available resources, but could include progression of the phosphate assets or development towards a once-a-day dose of Feraccru

Free cashflow



- The company is forecast to remain cashflow negative until substantial royalties are received from Feraccru sales across Europe and the US
- 2018 was affected by the greater-than-anticipated expense of a re-analysis of the AEGIS-CKD trial in February and March

Net cash/(debt) & capital increases



- At IPO in 2016, STX raised £32.5m gross (£30.1m net); in fiscal 2017, cash resources were boosted by a Placing of new Ordinary shares to raise £12.5m gross (£11.9m net).
- The commercial deal with Norgine significantly boosted STX's cash position towards the end of fiscal 2018, with the £11.0m upfront payment leaving cash on 31 December 2018 at £9.8m.
- Given the scheduled paediatric study, STX will require more funds in the future, which could come from one, or a combination, of equity, debt or licensing/distribution deals.

Source: Company data; Hardman & Co Life Sciences Research

Initiation of coverage

This report presents our valuation of Shield Therapeutics. It follows on from our introduction note '*Cast-iron investment*' on 28 January 2019[1], which summarised STX and its strategy. As detailed below, the context of the iron supplement market and reimbursement environment is crucial in understanding STX's value. The ability to execute on the regulatory and commercial strategies will be the biggest value drivers.

Investment thesis

Feraccru represents an important addition to the $3.4bn iron supplement market…

STX has a solid product that has obvious advantages for a large patient population underserved by current therapies. The safety of Feraccru has been demonstrated both in the clinic and in real world use, and it has been proven to be effective in improving iron levels with a sustained benefit in three Phase III trials. The risk lies in its commercialisation. Prescription iron supplementation is an established market worth $3.4bn (gross), dominated by cheap-to-produce and cheap-to-prescribe generic iron tablets. For patients in which iron tablets are not suitable, largely due to tolerability issues or the severity of iron deficiency, the treatment of choice is currently intravenous (IV) iron supplementation. IV iron is vastly more expensive than oral tablets and, as such, it accounts for 67% of the market by ex-factory sales (net), whilst accounting for only ca.10% of prescriptions. IV iron has also the major disadvantage of having to be administered in the hospital/specialist clinic setting because of the risk, albeit low, of causing anaphylaxis. The choice for STX on launch is to drive large sales volumes (and compete with established oral products in a wide range of iron-deficient patient sub-groups) with only a small price advantage, or to position Feraccru as a higher price alternative (difficult in the oral market given the established position of existing tablets and global pricing pressures).

…being a realistic oral alternative to IV iron that has to be administered in a hospital setting

There is a large pool of patient receiving IV iron due to tolerability issues with existing oral formulations

It's real opportunity, at least in the near-to-medium term, lies in the pool of IV patients who are taking this treatment approach due to tolerability issues with existing oral products, and in those patients who remain untreated for the same reason. This means that the initial target population, in which Feraccru must become established in order to succeed in penetrating the larger primary care market, is relatively small, despite representing a large commercial opportunity. Successful execution, therefore, requires careful clinical, pricing and market access strategies, along with careful timing of payer negotiations and commercial launches, to achieve optimal pricing across different markets. STX needs expert commercialisation partners with the necessary resources and who can access specialist clinicians (such as nephrologists and gastroenterologists) for accurate promotion.

STX is a low risk proposition with success dependent on execution of commercial strategy

What this means for STX is that success, delivered via licensing agreements, is all in the execution. Rollout must be efficient to reach peak market penetration before any future competition erodes sales. Therefore, the immediate challenge for STX's management is delivery on commercial strategy. Although this will be influenced by factors that are beyond its control, such as the time taken for regulatory and reimbursement approvals and patent objections from the competition, it will be greatly influenced by securing the right commercialisation partners. Overall, however, as highlighted in the executive summary (see page 3), the STX investment proposition is straightforward since Feraccru is approved and selling in Europe (currently Germany, the UK, Scandinavia) and is awaiting regulatory approval in the US.

[1] https://www.hardmanandco.com/wp-content/uploads/2019/01/Shield-Therapeutics-Cast-iron-investment-28.01.19.pdf

Clinically de-risked

Fortified for growth in Europe

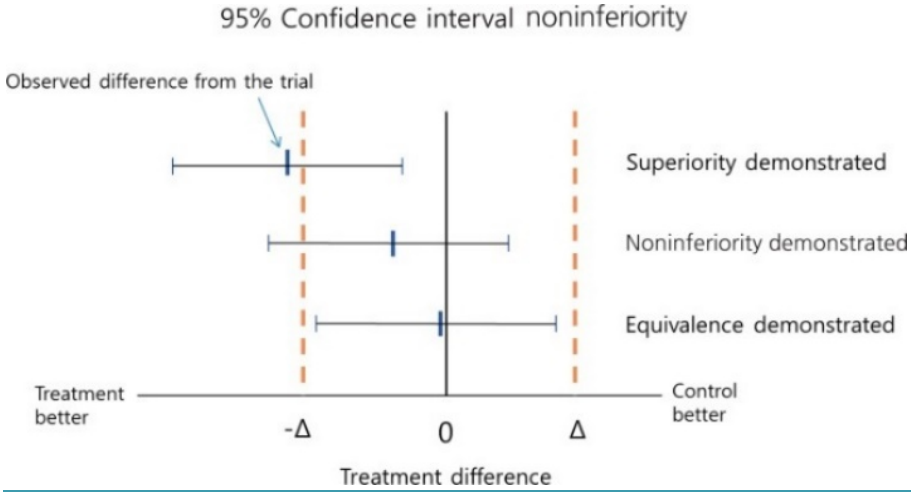
The recently reported successful outcome of the AEGIS-H2H study came as a big positive for STX and partners as, most importantly, the results will strengthen their position in negotiating reimbursement agreements for Feraccru in remaining European countries awaiting launch. Although the positive results are not expected to have an equal effect on US pricing, they do reduce the uncertainty surrounding the ability to achieve a higher list price (should the FDA approve Feraccru) and validate the product profile. The remaining countries covered by the Norgine, AOP Orphan and Ewopharma agreements, including the major markets of Spain, Italy and France, require reimbursement to be agreed prior to launch. Therefore, this achievement feeds directly into progressing Feraccru sales growth, and thus lifts our valuation. On the morning these results were reported, the market responded accordingly, with a clear 23% increase in share price (from 54.3p to 66.8p).

Results from head-to-head (H2H) study

Feraccru was non-inferior to IV iron in a well-controlled head-to-head study

The AEGIS-H2H followed a non-inferiority trial design, which is more complex to execute and interpret than conventional superiority studies. The positive outcome, therefore, also reflects well on STX's development team and clinical research organisation. Non-inferiority studies test whether a new treatment approach is not unacceptably less efficacious than an existing treatment, administered as an active control. The primary reason for carrying out this type of study was to allow STX to demonstrate the comparable efficacy of Feraccru with the market-leading IV iron (Ferinject; Vifor Pharma) in a defined patient population – those receiving IV treatment for iron deficiency anaemia (IDA) in inflammatory bowel disease (IBD) – so as to strengthen Feraccru's position in negotiating an optimal price with reimbursement bodies in Europe. Combined with prior studies, this will also aid clinical adoption in the target patient segment.

Non-inferiority analysis



Δ: margin for equivalence/non-inferiority.
Source: S. Hahn (2012) Korean J. Pediatrics

Feraccru at least as good as market leader, which had global sales of $762m in 2018

To demonstrate non-inferiority, a clinical response margin is prospectively defined, within which both treatment and active control must fall to be 'clinically equivalent'. A response in the AEGIS-H2H study was defined as normalisation of, or a ≥2g/dL increase in, haemoglobin (Hb) levels, and this had to be within 20% of Ferinject's response in either direction. There was a 9% difference in the number of responders in each arm, and these were within the 20% margin (statistically significant at

p=0.022). As Ferinject is the market-leading IV iron treatment, with in-market sales of $762m in 2018, non-inferiority status allows STX to negotiate for a price at the higher end of the range between oral and IV therapies. Peer-reviewed data are expected to be reported at scientific meetings later in 2019.

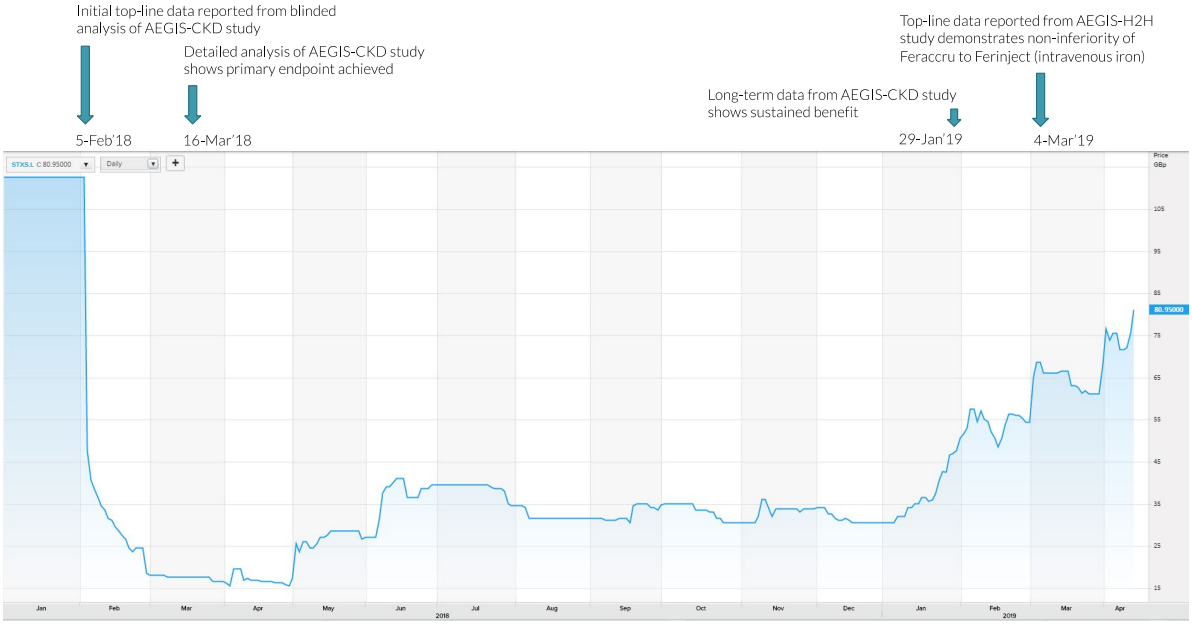
Lessons learned

Battle scars in chronic kidney disease (CKD)

The share price jump on the reporting of the top-line AEGIS-H2H data also reflects some recovery in sentiment following the loss of confidence that ensued from the preliminary AEGIS-CKD study reported on 5 February 2018, when management took the decision to carry out interim analysis of the AEGIS-CKD data at the end of the first study phase, at 16-weeks of treatment. Unfortunately, unbeknown to both the independent statisticians and STX (the data were blinded as per protocol), the 16-week readout included confounding data (such as patients who had undergone withdrawal events like rescue treatment with IV iron or bleeding events unconnected to treatment, but who had remained in the study). It appeared on first pass that Feraccru had not met its primary endpoint of a statistically significant increase in Hb levels compared with placebo. As shown in the chart below, this resulted in a share price crash of 58% (from 112.5p to 47.5p) on the announcement and this erosion continued to a low of 15.5p by the end of April 2018.

Despite the release of positive, and correct, results in March 2018 following detailed analysis of the unblinded trial data, the stock did not regain its previous market value and the share price has hovered at around 30p for the best part of a year, even with positive news from the EMA (which expanded Feraccru's label to all adult ID patients), signing of the licence agreement with Norgine, and, significantly, the FDA's acceptance of the AEGIS-CKD study for consideration for regulatory approval. There had been some uncertainty as to whether the FDA would accept a 'second go' at analysis. More than one year on, share price recovery is not complete and it is our view that complete recovery will not occur until a positive decision is made by the FDA for US approval (deadline: 27 July 2019).

Effect of AEGIS study read-outs on STX share price



Source: Hardman & Co Life Sciences Research

Positive AEGIS-CKD study results

The prospective statistical analysis of the full unblinded data set clearly showed that the primary endpoint had been met once confounding data were accounted for. Feraccru treatment resulted in a statistically significant (p=0.015) increase in Hb levels (mean change of 0.52g/dL) compared with placebo. Many of the secondary endpoints (importantly including other iron parameters) were also achieved, along with clear evidence that Feraccru treatment was well tolerated. As mentioned, this analysis was accepted by the FDA on submission of a New Drug Application (NDA) in December 2018, with which STX has applied for a broad label indication in line with that already granted in the EU and Switzerland.

In January 2019, these findings were reaffirmed in analysis of the second and final phase of AEGIS-CKD. The increase in Hb levels at 16 weeks (mean 0.57g/dL) were maintained during the additional 36-week open-label extension phase, and patients who had received placebo in the first phase experienced a comparable increase in Hb levels in their first 16 weeks of treatment. Feraccru clearly demonstrated good tolerability and 73.6% of patients remained on treatment with Feraccru out to the full 52 weeks of treatment.

AEGIS-IBD pivotal trial

Comparison with AEGIS-CKD results

Although a like-for-like comparison between the pivotal Phase III AEGIS-CKD trial and the pivotal Phase III AEGIS-IBD trial (completed in 2013) based on the publicly available data is not appropriate, the increase in Hb levels in IBD patients (ca.2.26g/dL) when treated with Feraccru was noticeably greater than in CKD patients (ca.0.57g/dL). A major factor is the different erythropoietin (EPO) profiles of the two diseases, with IBD patients generally having normal levels but CKD patients showing reduced EPO as disease severity increases. The Hb response is driven by EPO (which stimulates red blood cell production in the bone marrow); thus, it follows that Hb levels in AEGIS-CKD were limited by insufficient EPO. Moreover, Hb level increases were consistent with other CKD studies.

To fully understand the comparability of Feraccru efficacy between the IBD and CKD trials, a comparison of iron store replenishment secondary endpoints would be required. These have not yet been fully reported from the AEGIS-CKD study.

Summary of completed Feraccru clinical and outcomes studies

Trial name	Details	Top-line data and primary endpoint	Top-line data read-out
AEGIS-IBD	Pivotal trial submitted to EMA and FDA Adult IBD patients with IDA intolerant of other oral therapies Placebo-controlled	Hb increase of 2.3g/dL within 12 weeks (p<0.0001) Excellent outcomes: 97% compliance levels Safe and no evidence of iron overload	Complete (late 2013)
AEGIS-CKD	Pivotal trial submitted to FDA Adult CKD patients with IDA	Hb change of 0.6g/dL from baseline at 16 weeks Safe and no evidence of iron overload	Complete (March 2018)
AEGIS-PAED	Phase I, pharmacokinetics study (dose finding) Patients 12-17 years with ID	Positive efficacy data – serum iron parameters met Good tolerance at all doses	Complete (June 2018)
FRESH study	Real-world effectiveness of Feraccru in hospital practice	Feraccru real-world outcomes were similar to outcomes in the controlled AEGIS-IBD trial	Complete (June 2018)
AEGIS-H2H	Phase IIIb Head-to-head comparison with IV ferric carboxymaltose Adult IBD patients with IDA	Hb change from baseline at 12 weeks Feraccru demonstrated to be non-inferior to IV iron (Ferinject), within 9% of response to Ferinject treatment	Complete (March 2019)

CKD: chronic kidney disease, Hb: Hb, IV: intravenous,
Source: Hardman & Co Life Sciences Research

An important indication

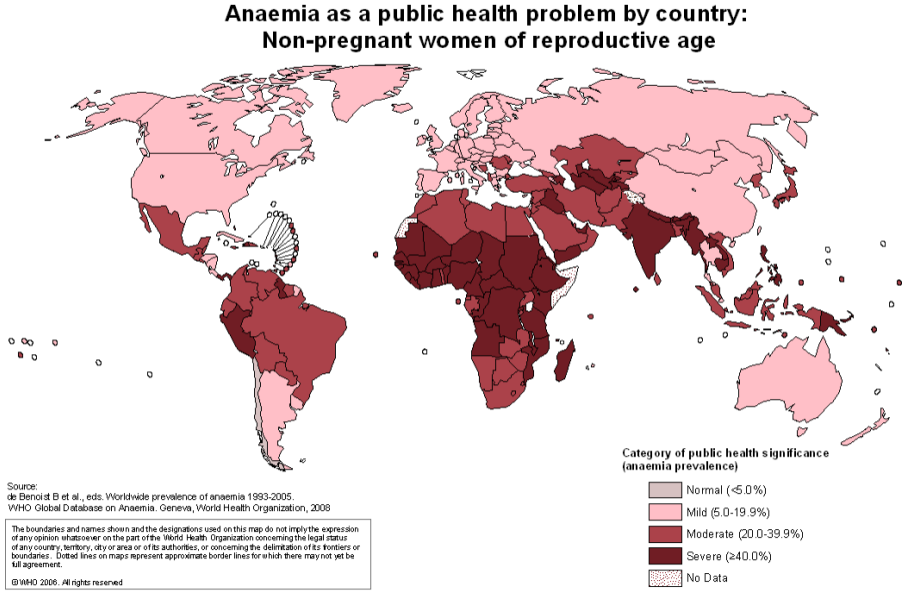
Simple doesn't mean boring

Iron is a low-risk product…

…that plays a vital role in normal body functioning

Iron is ubiquitous in the body and is particularly important in its role in the synthesis of Hb, which transports oxygen in red blood cells. Many people take off-the-shelf iron supplements as a measure to prevent fatigue, a widely-known effect of iron deficiency (ID). Although the use of iron supplements is widespread in developed countries and has a relatively simple scientific basis, ID is a significant global health problem, representing a large opportunity that is not to be underestimated. The Gates Foundation estimates that nutrition-related issues relate to 45% of child deaths under the age of five years, globally. Poor nutrition impairs neurological function, and even mild levels of ID can affect memory performance. ID is also associated with vitamin deficiencies (for example, vitamin C is required for iron absorption) and chronic conditions such as CKD, heart failure or IBD. The symptoms of ID are not specific and may develop slowly, so that they may not be readily recognised, with even iron deficiency anaemia (IDA) being underdiagnosed in high-risk patients.

Global prevalence of anaemia in women



Approximately 50% of anaemia worldwide is caused by iron deficiency
Source: World Health Organisation

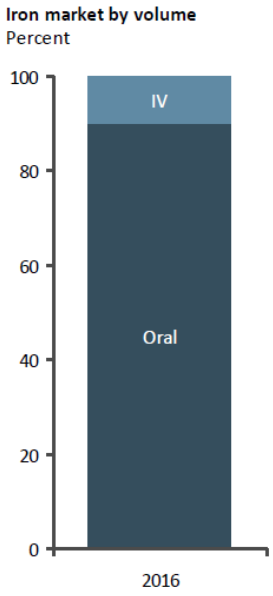
Prevalence of iron deficiency anaemia

ID has a global prevalence of 4%-12% in adults, with IDA affecting about half (2%-5%) of these adult male and postmenopausal female patients. Anaemia is defined as an Hb level below 12g/dL in females and 13g/dL in males, and its most common single cause worldwide is extreme ID, a condition in which there are no mobilisable iron stores and where there is evidence of a compromised supply of iron to tissues. The prevalence of ID and IDA is expected to grow as aging populations drive an increase in chronic disorders.

Feraccru was originally approved for use in adult IBD patients with IDA in the EU and now has an expanded indication to all adult patients with ID, with or without anaemia, in both the EU and Switzerland. In totality, this presents an opportunity of up to 40m patients.

Large and growing iron market

Iron supplement market



IV: intravenous
Source: Shield Therapeutics

Iron replacement

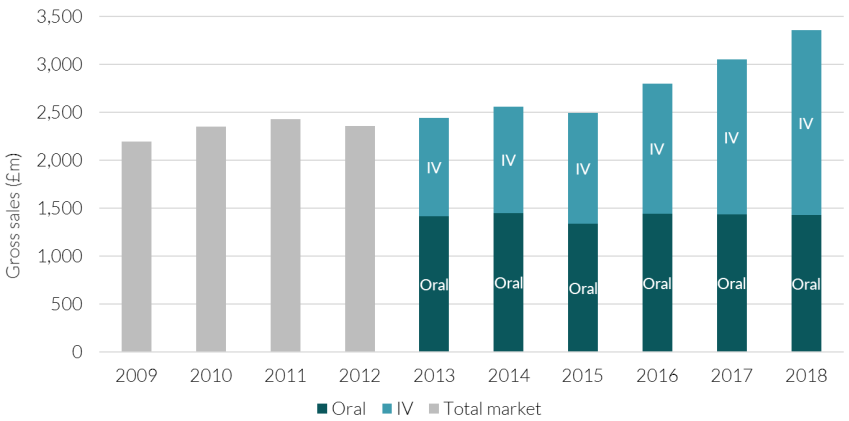
ID is treated through iron replacement therapy, using either oral products or IV administration. Although possibly restoring iron levels more rapidly compared with existing oral therapies, IV iron is inconvenient and expensive, and must be administered in hospital due to the risk of iron overload and life-threatening allergic reactions. Salt-based oral therapies, on the other hand, are extremely cheap and accessible; however, they are limited by poor tolerability in the gut and slower efficacy due to less efficient absorption, both of which lead to poor compliance.

The vast majority of available oral iron therapies are branded and generic iron salts such as ferrous (Fe^{2+}) fumarate and ferrous sulphate. Their accessibility and low price meant that the market was composed 85%-90% of oral therapies by volume in 2016 (STX data). Maltofer (ferric (Fe^{3+})-polymaltose complex, Vifor Pharma) is an oral formulation that was launched in the 1970s and, although it is not commercially available in major markets, its reported sales were $63m in 2018. In our opinion, it does not present much competition to Feraccru due to its relative lack of efficacy.

Market worth $3.4bn (gross) in 2018

Hardman & Co estimates that gross global sales of iron supplements were ca.$3.4bn in 2018. In contrast to market volumes (margin chart), sales are split 57%:43%, respectively, between IV and oral products due to the pricing differential, as seen in the following graphic. Whilst oral sales have been flat since 2013, revenues from IV iron therapies have increased in recent years, driven by a combination of: price rises; the underlying epidemiology; and improved diagnosis and treatment adoption rates among clinicians. The latter has been aided by significant education and promotional efforts by the market leaders such as Vifor Pharma.

Iron supplement market by sales



Source: Hardman & Co Life Sciences Research

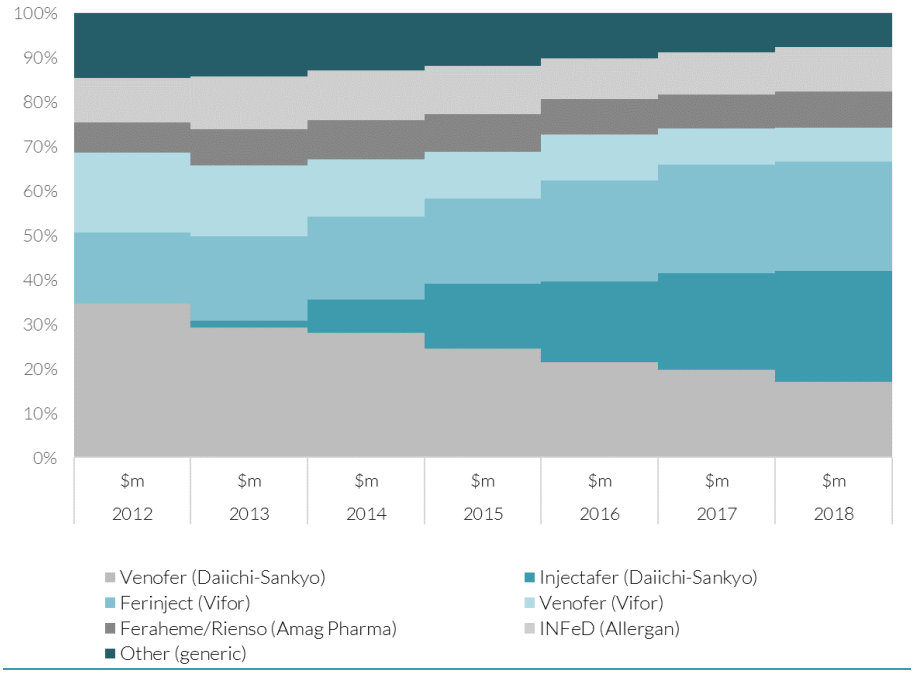
In-market discounts and rebates reduce the global size to $2.3bn based on ex-factory sales

Based on ex-factory sales, which allow for the discounts and rebates available to wholesalers, pharmacy benefit managers and other payers, the size of the net global market was $2.3bn in 2018, suggesting that the average discount across all products was 33%. There is a clear differential between the discounts available on IV products (22%) and existing oral products (47%). In our opinion, the improved treatment options provided by Feraccru are likely to see in-market discounts and rebates similar to the level seen with IV products. STX receives royalties based on net sales of Feraccru.

Competition in the IV iron market

The iron supplement market is relatively mature. The first IV iron infusion products in the 1960s were based on high molecular weight iron dextran complexes such as Imferon (removed from the market by Fisons for safety and/or economic reasons, depending on the source of information, in the mid-1990s). Low molecular weight iron dextrans (e.g. INFeD, Allergan) started to come on to the market about this time, which had a better safety profile; however, these were quickly superseded by the new class of ferric sugar complex formulations, which have a more favourable toxicity profile.

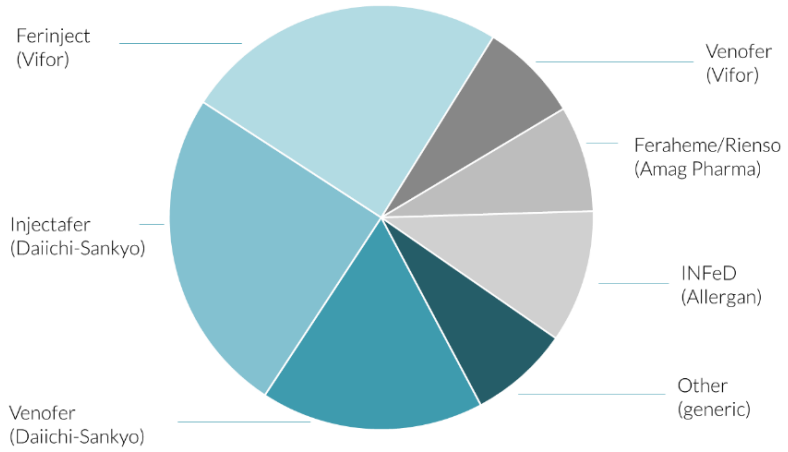
Evolution of IV iron market



Double counting of Ferinject/Injectafer sales, shared by Vifor and Daiichi-Sankyo, removed.
Source: Hardman & Co Life Sciences Research

The latest IV products have the benefit of reduced administration time, increased dose per infusion, and administration via 'IV push' – whereby a syringe is used to administer a one-time dose into the bloodstream. An example is Ferinject/Injectafer (ferric carboxymaltose), which is Feraccru's biggest competitor. This product is sold under the brand name Injectafer by American Regent (Daiichi-Sankyo) in the US, and as Ferinject in the rest of the world by Vifor. Combined ex-factory sales, excluding the double counting of US sales, of Ferinject/Injectafer were $762m in 2018, representing just over 50% of the IV iron market.

IV iron market 2018 – global total $1. 5bn (ex-factory)



Note: Double counting of Ferinject/Injectafer US sales, shared by Vifor and Daiichi-Sankyo, removed
Source: Hardman & Co Life Sciences Research

Note that the market could include products like Venofer (iron sucrose), which is now largely only used in the relatively small renal dialysis patient population. Also, although we do not view phosphate binders as competitors to Feraccru, in 2017 the FDA approved Auryxia (Akebia-Keryx) for treatment of IDA in CKD. Finally, some erythropoiesis-simulating agents (ESAs), while not direct competitors and even complementary to Feraccru, may increase Hb to levels at which less iron supplementation is used.

All in the execution

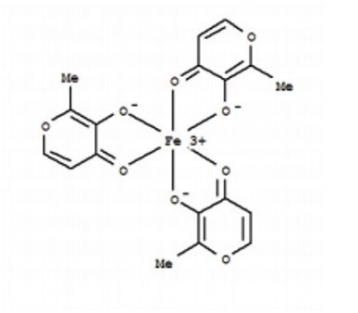
Product positioning crucial

Feraccru has a differentiated tolerability profile that lends itself to an unmet need within existing treatment pathways. In valuing STX, we have made assumptions on the company's commercial strategy and that of its commercialisation partners, including the timing and sequence of: launches into new markets; future clinical and outcomes studies; and likely penetration of target markets.

Feraccru's potential in Europe has been validated by the signing of the Norgine agreement. Complete value delivery depends on the successful execution of full commercialisation at the right price.

Feraccru – improved tolerability

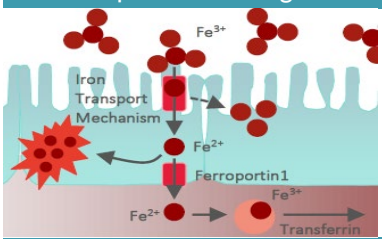
Ferric maltol



Source: European Medicines Agency, 2015

Feraccru answers the tolerability issues of existing oral therapies on the basis of its chemical structure. Feraccru (ferric maltol) is a complex of an Fe^{3+} ion and three maltol (sugar) molecules that remains stable and in solution in the GI tract, only dissociating into maltol and iron when it is taken up by the cells lining the gut. It is delivered in a capsule formulation, making it straightforward to administer, transport, and store. Unlike Feraccru, the iron in salt-based oral iron formulations is required to disassociate from its carrier salt before it able to be absorbed and become available to the body's iron transport mechanism. This dissociation forms insoluble products that collect (agglomerate) in the gut causing constipation, and it produces hydroxyl free radicals via the Fenton Reaction, which irritate the gut lining. It can also reduce the efficiency of iron uptake. Since Fe^{3+} in Feraccru is in a form that is more accessible to the cells lining the gut, its uptake is naturally regulated according to need. Iron is stored in the liver and bone marrow, among other sites, and is released and sequestered among compartments in a highly dynamic process. When treatment with Feraccru begins, the rate of restoration of iron stores depends on ID severity, with erythropoiesis prioritised if Hb is low. Any unabsorbed Feraccru simply transits through the gut and is excreted as 'inert' ferric maltol.

Iron transport in human gut



Source: Shield Therapeutics Investor Materials

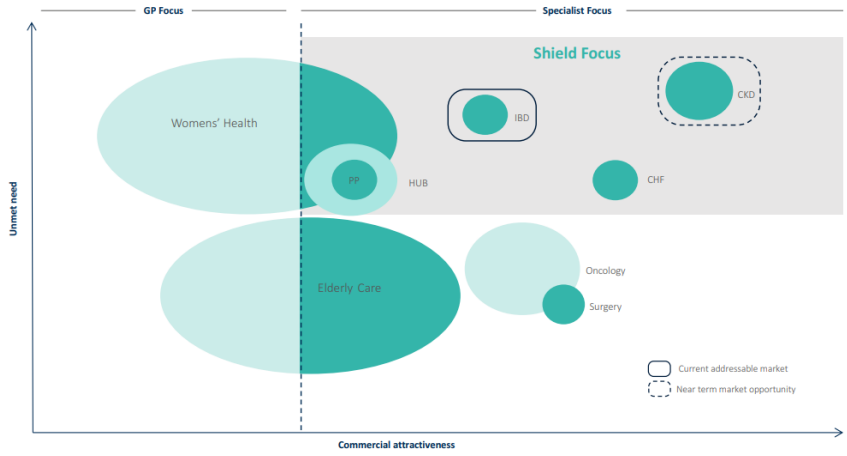
Product strategy

To capture a decent share of a competitive (but relatively poorly penetrated) $2.5bn (net) iron supplement market, STX and its commercial partners must ensure that the benefits of Feraccru® in comparison with both salt-based oral irons and IV irons are effectively and robustly communicated. In turn, this will help Shield and its partners achieve good initial pricing for Feraccru in the broader European and US healthcare markets, expanding on the premium pricing already achieved in the UK, Germany and Scandinavia. This means, by definition, that Feraccru® is not positioned as direct competition to existing oral therapies (despite offering tolerability advantages) as the required lower price point would not provide an attractive commercial opportunity, or alternatively, the high price point would draw the unwanted attention of national reimbursement agencies due to the potential budget impact related to the large volume of oral salt-based iron prescriptions. Moreover, initial positioning of Feraccru® as the answer to general ID in primary care settings would be difficult to achieve, expensive, and take time to show traction.

Attractive commercial opportunity and high unmet need in Inflammatory bowel disease (IBD) and chronic kidney disease (CKD

Therefore, STX is taking the approach of first establishing Feraccru® in specialist care through promotion to key opinion leaders (KOLs). Adoption should then trickle down into the primary care setting, at which point the premium price of Feraccru might come under pressure in the European market. To ensure good penetration of the specialist market, STX is initially targeting IBD and CKD, in which gastroenterologists and nephrologists have good awareness of the propensity for iron deficiency anaemia, and who are familiar with the tolerability, risk and cost issues associated with existing treatment options.

Shield's target market in iron deficiency

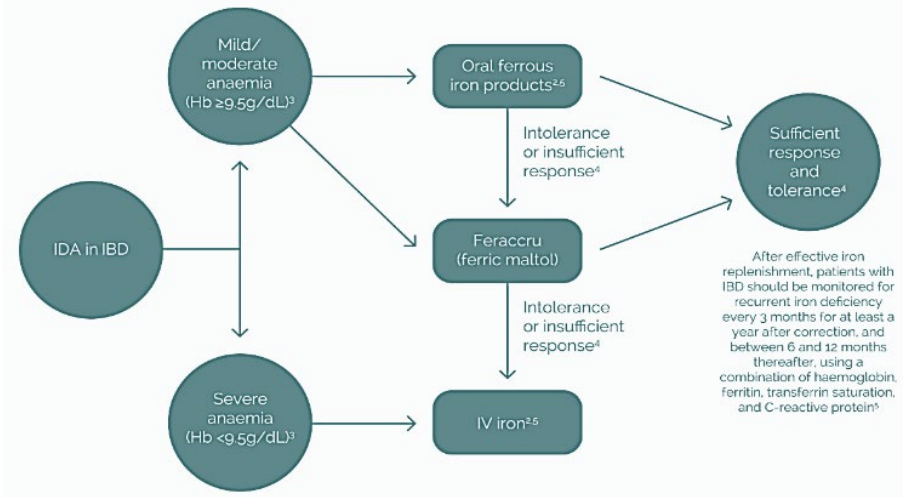


HUB: heavy uterine bleeding; PP: post-partum; CHF: congestive heart failure
Source: Shield Therapeutics

Existing treatment pathway

Approximately 24% of patients with IDA in CKD and IBD chronic disorders are treated with IV iron, normally after unsuccessful treatment with existing salt-based oral iron products. Feraccru thus fits easily with existing medical practice as second-line treatment following existing orals and instead of IV. As its benefits become more widely known, it may also be adopted as a first-line treatment in these disorders, as in the diagram below. It is less likely to be adopted as a first-line option in severe cases of IDA in IBD and CKD due to the speed with which iron levels must be restored, as for such patients a blood transfusion is the treatment of choice being the only therapeutic option that gives a rapid increase in Hb levels.

Feraccru treatment pathway for IDA in IBD



Source: Shield Therapeutics

Feraccru is already being sold in the UK, Germany and a number of other small EU countries and, although NICE in the UK has not provided recommendations, Feraccru has been incorporated into various NHS Trust policies and hospital formularies, which is good validation that this strategy is working. Real-world evidence was recently generated in the FRESH study at seven UK hospitals, with encouraging results: 62% of patients had normalised Hb levels following treatment with Feraccru, which was similar to those seen in the pivotal phase 3 AEGIS-IBD study.

Pricing and launch strategy

Pricing strategy

In Europe, the relationship between adoption of a new medicine like Feraccru and its price is relatively inelastic due to the control of government payers in each country. Feraccru has successfully achieved good pricing and reimbursement agreements with some clinical commissioning groups (CCGs) in England and is approved for reimbursement in Germany on a national basis, where each pack (28-day course) is agreed at £47.60 or €64.00, respectively. In terms of health economics data, a London NHS Trust has recently demonstrated that treatment with Feraccru instead of IV iron would save the Trust more than £250k each year and more than 107 days of nursing time. Most important, the recent positive results (discussed on page 6) from the AEGIS-H2H non-inferiority study against IV iron position Norgine very strongly towards achieving a Germany/UK level price in the remainder of Europe.

Should demand for Feraccru in primary care pass a certain point in the future, there is the potential for pricing pressure from European payers to increase, with bodies such as NICE in the UK becoming more demanding of health outcomes studies. It is possible that Norgine may wish to carry out further studies to support negotiations in coming years across Europe; for instance, undertaking a head-to-head study against oral iron. STX does, however, retain the power to veto such projects if they affect its activities elsewhere, in addition to being responsible for undertaking and funding certain further developments. For example, STX may work towards developing a once-a-day formulation, although this is likely to be delayed until commercial launch is under way in the US.

STX has more pricing power in the US market, where the price-demand relationship is less sensitive. It is our opinion that Feraccru is unlikely to achieve price parity with IV iron, although its advantages to payers in terms of the overall costs of IV treatment are likely to position it favourably towards the upper end of the oral-IV treatment-only price range. In addition, and in contrast to Europe, the price of Feraccru is more likely to increase year-on-year. Setting the right initial price is important in avoiding market access restrictions through too low a tier (incurring patient co-pays) or too high a tier, whereby Feraccru is unlikely to be substituted for alternative treatments.

Global rollout

Whether peak sales are reached is dependent on the efficiency of rollout within the period of market exclusivity and prior to patent expiry (currently 2035). This depends on management's ability to close good commercialisation deals in the US and on STX's partners' ability to successfully promote and secure pricing agreements for Feraccru in the remaining European countries, the US, and Australia and New Zealand. Due to the longer time needed for this process in Europe, we assume that peak sales in both Europe and the US could be reached by 2027 in the initial target market. Should the FDA approve Feraccru, we expect first US sales in 2020, contingent on a partner being signed in 2019, as expected.

Strategy validated by commercialisation partners

Three commercialisation partners:

- Norgine (EU/Australia/New Zealand)
- AOP Orphan Pharmaceuticals AG (Scandinavia)
- Ewopharma AG (Switzerland)

STX's out-licensing strategy for commercialisation is proving successful, with three partners signed in Europe. These provide early but meaningful validation of the managements' approach. Despite reduced marketing spend prior to signing the Norgine agreement, modest sales growth was achieved by STX in the UK and Germany, demonstrating demand for Feraccru. The Norgine agreement was signed in September 2018, granting it an exclusive commercial licence to Feraccru in Europe (in territories not covered by STX's existing partners AOP and Ewopharma), and Australia and New Zealand for the duration of patent protection. STX retains the IP and responsibility for the manufacture and supply of Feraccru, and all aspects of its development, with payments available on development and sales milestones (such as successful completion of the Phase III paediatric study). The financial terms were:

- £11m upfront licence payment to STX;
- a potential total of €54.5m in development and sales milestones; and
- tiered royalties of between 25% and 40% on Norgine's sales.

Peak sales potential

Peak sales estimates

Taking the above into account, we have estimated peak sales for Feraccru in IBD and CKD patients diagnosed with IDA in Europe and the US, where initial promotional efforts will be focused. The US opportunity is ca.2.5x that of Europe despite the smaller pool of patients, and the CKD opportunity is ca.2.3x that of IBD. Our total estimated peak sales are ca.$640m/£490m in these indications; however, should approval be granted for general ID, the potential is clearly greater.

We conclude that an approval in the US market and particularly the CKD label will be the biggest driver of value. Within this, the price achieved for Feraccru and successful execution of the commercialisation strategy are the remaining risks.

Target patient populations and peak sales

Condition	Potential Feraccru patients*†			Peak sales potential*	
	Oral IDA therapy	IV IDA therapy	IDA untreated	$m	£m
Diagnosed non-severe IBD	12,500	72,600	90,700	195	148
Europe	7,700	44,900	56,200	55	42
US	4,800	27,600	34,600	140	106
Diagnosed CKD, stages 2-4	20,800	85,200	301,800	445	340
Europe	11,900	69,300	173,200	130	99
US	8,900	15,900	128,500	315	242
Total				**640**	**490**

**Rounded numbers. See references for epidemiological sources.*
†Based on penetration rate estimates per treatment segment
Source: Hardman & Co Life Sciences Research

Peak sales assumptions

Assumptions have been generated from our understanding of STX's commercial strategy in the context of the current industry landscape. Expansion into primary care settings and general iron deficiency, or into dialysis patients, has not been modelled at this point, and these estimates are therefore conservative.

- **Patient populations:** Adult and paediatric patients with non-severe IBD or stage 2-4 CKD with IDA.
- **Diagnosis rates:** Assumed to be ca.50% of these IBD patients and ca.40% of these CKD patients.
- **Dose**: Patients take Feraccru twice daily, every day, for an average of six months per annum (e.g. as two 12-week courses[2]).
- **Current patient segments:** 31%, 24%, 45% patients on oral iron, IV iron, and untreated, respectively (Shield Therapeutics & ECCO Guidelines 2017[3]). Estimated average penetration of 18% and 12% for Feraccru for first and second-line treatment across treatment segments in IBD and CKD, respectively, indicating that Feraccru will grow the iron supplement market.
- **Competition:** No new direct competition assumed.

[2] New Medicine Policy Recommendation, NHS Lancashire Medicines Management Group
[3] ECCO Guideline/Consensus Paper J Crohn's Colitis 2017:769-784

- **Distribution:** We have assumed that additional deal(s) will be signed to cover the US and that existing commercialisation partners have full European coverage.
- **Price estimates:** Assuming two three-month courses per year, we estimate revenues of €425/£380 per patient per year in Europe and $2,100/£1,615 per patient per year in the US (ca.80% of 'in market' IV iron price).

Operational progress

Operational progress and expected near-term news

Date	Event	Significance
Feb'16	European approval granted for IDA in IBD	Feraccru safe and effective
2016	Licence agreement with AOP Pharmaceuticals	Accelerates Feraccru commercialisation in Europe
Jun'16	UK launch	The first launch
Jul'17	Ewopharma licence agreement	Accelerates Feraccru commercialisation in Europe
Feb'18	Efficacy endpoint in blinded top-line AEGIS-CKD study data not statistically significant	Issues from inclusion of data from protocol violators
Mar'18	EU Commission broadens Feraccru label to all adults with ID	Greatly expands potential market to >40m patients
Mar'18	Statistical significance from AEGIS-CKD study on analysis of full unblinded data (confounding data treated according to prospective SAP)	Data for NDA submission to FDA
Jun'18	Positive PK data from Phase I paediatric study	Stepping stone to a global Phase III study in paediatric patients
Sep'18	Licence agreement with Norgine for Feraccru commercialisation (maximum €65.5m)	Accelerates commercialisation
1Q'19	Preliminary results from AEGIS-H2H study	Feraccru non-inferior to IV iron
Apr'19	Extension to Swiss approval of Feraccru label to all adults with ID	Further validation of clinical utility
27 Jul'19	**FDA decision (PDUFA) deadline**	**Approval in the US opens up the large US market**
2H'19E	Start recruitment Phase III paediatric study	Towards expanding Feraccru's label
Ongoing	Further potential licensing agreements	Accelerating commercialisation and geographical expansion

CKD: chronic kidney disease, IDA: iron deficiency anaemia. IBD: inflammatory bowel disease
NDA=New Drug Application, SAP = Statistical Analysis Plan
Source: Hardman & Co Life Sciences Research

Intellectual property

Summary Feraccru IP

Feraccru technology was discovered by Vitra Pharmaceuticals in the 1990s. Following research at St Thomas' Hospital, London, it was further developed and patent applications, including those covering manufacture, were submitted prior to 2010. STX acquired Feraccru's IP in 2010: a royalty of up to 5% is due to Vitra on net sales of Feraccru. Since 2010, STX has filed five new patent applications and one term extension related to the EU approval, which together should grant protection up to 2035. In total, Feraccru is protected by a broad suit of nine patent families, including those involving dosing regimen and manufacture. STX also owns a series of blocking patents designed to cover alternative methods of manufacture.

Patent objections

In January 2019, objections were submitted to the European Patent Office (EPO) by Teva concerning two recently submitted patents that cover Feraccru manufacture, and which expire in 2032 and 2035. The EPO has subsequently (in March 2019) reached a decision in favour of STX on the process patent. It should be noted that Teva

also filed objections in 2018 against patents concerning manufacture of Auryxia (Akebia).

Valuation

We have undertaken detailed analysis of STX to arrive at a risk-adjusted net present value (rNPV) of £194.2m, or £1.66/share. This was derived by DCF analysis of forecast cashflows to peak sales of key assets, informed by conservative assumptions.

DCF analysis

Cashflow forecasts (by commercial partners) were generated for each of Feraccru and PT20 from anticipated launch through to patent expiry, at which point net sales were assumed to fall 80% within a year as a result of generic competition. We use a weighted average cost of capital (WACC) of 10%.

STX's development portfolio

Although there are other products of interest in STX's proprietary portfolio, these are not the focus of this report. Since PT30 and PT40 are only at a very early stage of development and represent relatively small market opportunities, they contribute little to STX's rNPV.

PT20 is the bigger opportunity in the phosphate binder market, estimated at $1,022m in 2017 (Hardman & Co data). However, a large and expensive Phase III trial and probably a commercial partner are required to progress the asset. We have prepared a DCF model for PT20 based on the actual ex-factory sales achieved by commercially available phosphate binders from launch until patent expiry. These were: Renagel (Sanofi); Fosrenol (Shire); and Velphoro (Vifor Pharma). Applying a royalty rate of 15% (assuming out-licensing prior to Phase III) and a 40% clinical risk adjustment produced an rNPV of £0.12m. This relatively low value was also influenced by PT20's short lifetime assuming launch in 2022 and patent expiry in 2029, assuming that no extensions are available.

Risk-adjustments

Phase completed	Small molecule drug
Pre-clinical	1%
Phase I	5%
Phase IIa	20%
Phase IIb	40%
Phase III	80%
Regulatory submission	85%-90%

Source: Hardman & Co Life Sciences

Feraccru cashflow forecasts

Cashflow forecasts to peak sales of Feraccru in treatment of IDA in adult and paediatric IBD and CKD patients were prepared. It should be noted that for ease of comparison between the US and European opportunities, we have assumed that future commercialisation deals have a similar structure as the existing arrangement with Norgine. For the potential US cashflows, however, we assumed a lower COGS margin (of 8%, in contrast to 15% in Europe) due to the higher price points in the US market, and applied an 85% risk-adjustment for the uncertainty of US approval. The latter is at the lower end of average industry rates due to the previous, although now resolved, complications with the AEGIS-CKD trial in February and March 2018 (see page 7).

DCF summary

The rNPV of Feraccru is £184.3m. The opportunity in Europe alone is currently valued at £107m, and in the US alone is £77.0m. A US approval in both CKD and IBD would increase the latter considerably.

DCF summary

	rNPV	NPV/share
Feraccru in Europe only	£107m	£0.92
Feraccru in US only	£77m	£0.66
Feraccru	**£184m**	**£1.57**

Numbers may not add up exactly due to rounding
Source: Hardman & Co Life Sciences Research

DCF assumptions

Our valuation is likely to be conservative because, in addition to the assumptions made in drawing up the peak sales potential (see page 15), we have restricted cashflow forecasts as follows:

- **Target indications:** IDA in adults and children with IBD or CKD.
- **Time horizon:** Peak sales in both the US and Europe achieved by 2027, with patent protection up to and including 2035.
- **Feraccru pricing:** We have assumed that the Germany/UK price is achieved in the rest of Europe, and in the US is ca.80% of IV iron, and that this remains flat.
- **Risk adjustment:** Completely de-risked in Europe, 85% in the US.

Royalties and rates

STX's strategy is to partner its products for commercialisation. Thus far, these agreements have not been traditional distribution agreements, with STX instead receiving higher royalties on net sales by its partners, from which the cost of manufacture/supply must be deducted. Since the royalty and milestone tiers are undisclosed, we have applied our own assumptions, including royalties between 25% and 40% paid on sales tiers between £2m and £100m. We have not included future/unpaid development milestones (€2m for the Phase III paediatric trial) in our DCF given that the R&D spend needed to achieve them has also not been included.

Associated costs

In its existing agreements, STX has remained responsible for any further development activities and for the costs of regulatory approval. Moreover, STX is responsible for manufacture of Feraccru. COGS associated with the latter have been deducted from our cashflow forecasts and include the 5% royalty owed to Vitra. COGS fall to ca.12% in Europe once peak sales are achieved and remain at 8% in the US throughout.

Sum-of-the-parts

Pulling all this together in a sum-of-the parts analysis, we arrive at the following summary. Successful execution of the Feraccru commercialisation strategy has the potential to drive a highly satisfactory long-term royalty stream. On our estimates, Feraccru represents 95% of the group's present value. While there is much value in the European opportunity, approval and successful commercialisation in the US in both IBD and CKD will drive most of the future value of the group. As shown above, the rNPV in the US is eroded by risk that Feraccru does not reach the market.

In conclusion, STX has a risk-adjusted value of 166p/share, indicating considerable upside potential from a 94.7p share price (8 May 2019). Further positive news flow from the FDA on Feraccru – latest 27 July 2019 – would change the risk-adjustment and increase the valuation, at which point this share price could be reached relatively quickly.

Summary valuation	
Shield Therapeutics	**£m**
Feraccru royalty stream – risk adjusted	184.3
PT20 royalty stream – risk adjusted	0.1
Net cash/(debt)	9.8
Market capitalisation	194.2
Shares in issue (m)	117.0
Valuation/share (p)	166

Source: Hardman & Co Life Sciences Research

Valuation discussion

Uncertainties and risks

Peak sales estimates, cashflow forecasts and our resulting valuation of STX could be greatly affected by changes in the factors listed below.

- **Expanded indication:** Clinical adoption for general ID treatment in adults in Europe, which would be entirely appropriate given its label in the EU and Switzerland, would greatly increase cashflow forecasts.
- **Treatment duration:** Given that the Summary of Product Characteristics[4] (SmPC; part of marketing authorisation) states that treatment with Feraccru should continue as long as necessary to replenish iron stores, it is possible that chronic Feraccru therapy may become the norm in ID/IDA patients with chronic diseases such as CKD. This would also greatly increase cashflow forecasts.
- **Initial Feraccru price on launch:** Not achieving the estimated US price would have the biggest effect on the rNPV. It is likely that a price near that of the UK/German price will be achieved in the rest of Europe following the positive conclusion of the AEGIS-H2H study.
- **US label:** It is possible, although highly unlikely, that the FDA will initially approve Feraccru in IBD but not CKD. There is also the possibility of approval in general ID, with or without anaemia.
- **US deal:** We have made assumptions on the structure and size of a US deal for Feraccru – announcement of a deal after launch will result in a revised model.
- **Penetration rate:** We have assumed a certain level of adoption in target patient sub-segments based on our best knowledge and informed by the current composition of the IV iron market; once the product has been on the market for a longer period, we will have better visibility.
- **Changes in price over time:** e.g. declining prices in Europe (possible) and increasing prices in the US (probable).
- **Delays to paediatric approval:** Feraccru is not approved in paediatrics and delays to the Phase III study would alter the sales trajectory; however, we estimate the target population to include only ca.60,000 paediatric patients p.a. at peak.
- **New territories:** Launches in Australia, New Zealand, China, Japan or the Middle East/Africa, and associated commercialisation agreements, would result in an upgrade.
- **Growth in the underlying market:** Improved rates of IDA diagnosis due to education of the market would increase peak sales; we have not accounted for increasing prevalence of CKD or IBD in our model.
- **Competition:** We have not assumed the introduction of direct competition from new IV or oral iron therapies with a similar product profile.
- **Patent protection:** There is a chance that the recent objection to Feraccru's composition of matter patent by Teva will result in earlier competition from a generic version. This would reduce our valuation accordingly.

[4] https://www.ema.europa.eu/en/documents/presentation/presentation-introduction-summary-product-characteristics-smpc_en.pdf

Commercial scenarios

Scenario analysis (rNPV, £m)			
Scenario	Europe alone	US alone	Both
Estimated price successfully achieved	**107.4**	**77.0**	**184.3**
Suboptimal price achieved (55%-60% IV iron therapies)	103.6	67.9	169.2
Suboptimal price achieved in US (55%-60% IV iron therapies); Price drops to oral iron level after three years in Europe	24.0	67.9	82.4
Price drops to oral iron level after three years in Europe, suboptimal price achieved in IBD in US (55%-60% IV iron therapies); US label excludes CKD	16.7	42.6	57.1

Source: Hardman & Co Life Sciences Research

We believe that US approval in IBD and CKD and the price achieved for Feraccru in payer negotiations is the biggest driver of STX's success. The table below illustrates the impact of various theoretical regulatory and reimbursement scenarios.

Comparative valuation

We have attempted to put our estimate of the intrinsic value of STX into context by comparing it with its peers. The difficulty in arriving at a market valuation for STX is that it has no direct competitors. Therefore, we have used the best available global peers, all of which pose only a degree of competition to STX.

- **Vifor Pharma:** Formerly Galencia Group, Vifor is a well-established and experienced manufacturer of iron replacement and other pharmaceutical products, capitalised at CHF8.6bn/£6.3bn. This Swiss headquartered multi-national company manufactures Ferinject, the market-leading IV iron therapy and Feraccru's biggest competitor.
- **Amag Pharmaceuticals:** An established pharmaceuticals company headquartered in Massachusetts, US, specialising in anaemia, pregnancy and other women's health complications. Its IV iron therapy, Feraheme, holds ca.8% of the IV iron market. Between 2010 and 2014, Takeda held exclusive distribution rights to Feraheme/Rienso in Canada and Europe.
- **Akebia Therapeutics:** Recently merged with Keryx Biopharmaceuticals to form a company focused on kidney disease treatments, Akebia has a strong and growing presence in the phosphate binder space. Akebia markets Auryxia (ferric citrate tablets), which is indicated for control of phosphate levels in CKD dialysis patients in addition to IDA in adult patients not on dialysis.

Comparative valuation				
Table subtitle	Vifor Pharma VIFN	Amag Pharma AMAG	Akebia Therapeutics AKBA	Shield Therapeutics STX
Local currency	CHF	$	$	£
Share price	133.3	11.0	5.9	0.9
Shares in issue (m)	65.0	33.8	117.1	117.0
Market cap (lc)	8,664.5	371.4	689.8	110.9
Mkt cap (£m)	6,629.3	285.6	530.5	110.9
Cash	114.5	394.0	321.0	9.8
Debt	-310.6	-341.0	-15.0	0.0
EV (lc, m)	8,860.6	318.4	383.8	101.1
EV (£m)	**6,779.3**	**244.9**	**295.2**	**101.1**
EV relative to STX (x)	67.0	2.4	2.9	-

Prices taken at close of business on 8 May 2019
Source: Hardman & Co Life Sciences Research

- **Note:** AMAG's share price fell 18% to $11.29 on 8 March when one of its drugs (non-iron) failed in a confirmatory Phase III trial.

Conclusion

Given the size of both Vifor and Amag, a direct comparison with these companies is not realistic. However, the market does provide a benchmark for STX's current EV. We have not generated sales multiples because STX's cashflow is driven by royalties rather than conventional sales, but on the basis of relative EV alone, STX appears undervalued. Given Feraccru's benefits over existing commercialised IV and oral iron therapies, and the discrepancy between our rNPV/share of 166p and the current share price of 95p (8 May 2019), STX is an interesting investment opportunity, in our opinion.

Financials

Profit & Loss

- **Sales:** Up to 2018, product sales represent direct selling of Feraccru by Shield. In 2018, this figure (already reported) represents a combination of direct selling and sales to Norgine in Europe. In 2019 and beyond, sales are to partners only.
- **COGS:** Future costs reflect the costs of having Feraccru contract manufactured by a third party before shipment to a partner and include a 5% pay away to Vitra. The gross margin is expected to be ca.84%-85%.
- **SG&A:** In future, the SG&A figure will reflect the corporate overhead, given that STX will have no direct sales activity itself. No allowance has been made for potential legal costs regarding patent challenges.
- **R&D:** Management has flexibility regarding the timing of R&D spend to bring the phosphate products through trials. Short term, it will be accruing the costs of the recently concluded H2H trial and will begin the paediatric Phase III trial.
- **Milestones and royalties:** To ensure consistent treatment of milestones and royalties across all companies, which command a near-100% margin, these are included in 'other income'. STX is likely to include them within gross revenues.

Profit & Loss account					
Year-end Dec (£m)	2016	2017	2018E	2019E	2020E
GBP:EUR	1.18	1.14	1.14	1.14	1.14
GBP:USD	1.35	1.29	1.31	1.31	1.31
Gross revenues	0.34	0.64	11.88	2.83	2.00
Sales	0.30	0.64	0.86	0.63	2.00
COGS	-0.10	-0.16	-0.31	-0.40	-1.20
Gross profit	0.20	0.48	0.55	0.23	0.80
Gross margin	67.1%	75.7%	63.7%	84.0%	85.0%
SG&A (underlying)	-8.69	-14.12	-9.52	-4.44	-5.20
R&D	-2.03	-4.71	-4.30	-4.73	-2.51
EBITDA	-10.29	-17.92	-1.80	-6.30	-6.45
Depreciation	-0.01	-0.01	-0.01	-0.01	-0.01
Amortisation	-0.17	-0.42	-0.45	-0.45	-0.45
Other income	0.04	0.00	11.03	2.20	0.00
Underlying EBIT	**-10.47**	**-18.34**	**-2.25**	**-6.75**	**-6.90**
Share-based payments	-0.29	-0.56	-1.01	-1.01	-1.01
Exceptional items	-1.70	-2.05	-1.90	-1.90	-1.90
Statutory EBIT	-12.46	-20.95	-5.17	-9.67	-9.82
Net interest	0.04	0.00	0.02	0.02	-0.03
Forex gain/loss	0.27	-0.04	0.00	0.00	0.00
Underlying PBT	**-10.43**	**-18.35**	**-2.24**	**-6.73**	**-6.93**
Extraordinary items	0.00	0.00	0.00	0.00	0.00
Statutory PBT	-15.60	-20.99	-5.15	-9.65	-9.85
Tax payable/credit	0.59	1.41	3.36	0.45	0.45
Underlying net income	**-9.84**	**-16.94**	**1.12**	**-5.41**	**-6.55**
Statutory net income	-15.02	-19.59	-1.79	-9.20	-9.40
Ordinary 1.5p shares:					
Period-end (m)	108.14	116.43	117.04	117.04	117.04
Weighted average (m)	101.16	112.36	116.43	117.04	117.04
Fully-diluted (m)	101.16	112.36	116.53	117.24	117.34
Underlying basic EPS (p)	**-9.73**	**-15.08**	**0.96**	**-4.62**	**-5.60**
Statutory basic EPS (p)	-14.84	-17.43	-1.54	-7.86	-8.03
Underlying fully-dil. EPS (p)	-9.73	-15.08	0.96	-4.61	-5.59
Statutory fully-dil. EPS (p)	-14.84	-17.43	-1.54	-7.85	-8.01
DPS (p)	0.0	0.0	0.0	0.0	0.0

Source: Hardman & Co Life Sciences Research

Balance sheet

- **Cash position:** At IPO in 2016, STX raised £32.5m gross (£30.1m net); in fiscal 2017, cash resources were boosted by a Placing of new Ordinary shares to raise £12.5m gross (£11.9m net); and the commercial deal with Norgine significantly boosted STX's cash position towards the end of fiscal 2018, with the £11.0m upfront payment leaving cash on 31 December 2018 at £9.8m.
- **Norgine upfront:** In 1H'19, STX received a €2.5m/£2.2m development milestone payment linked to successful completion of the AEGIS-H2H study; this will support the Phase III paediatric study due to begin this year.
- **Asset-light:** STX has a virtual business model and the associated asset-light structure.

Balance sheet					
@31 Dec (£m)	**2016**	**2017**	**2018E**	**2019E**	**2020E**
Shareholders' funds	48.40	41.21	40.43	31.23	21.83
Cumulated goodwill	0.00	0.00	0.00	0.00	0.00
Total equity	48.40	41.21	40.43	31.23	21.83
Share capital	1.62	1.75	1.75	1.76	1.76
Reserves	46.77	39.46	38.68	29.47	20.08
Capitalised R&D	0.00	0.00	0.00	0.00	0.00
Minorities	0.00	0.00	0.00	0.00	0.00
Provisions/liabilities	0.00	0.26	0.00	0.00	0.00
Deferred tax	0.00	0.00	0.00	0.00	0.00
Long-term loans	0.00	0.00	0.00	0.00	0.00
Short-term debt	0.00	0.00	0.00	0.00	0.00
less: Cash	20.98	13.30	9.78	6.02	0.83
less: Deposits	0.00	0.00	0.00	0.00	0.00
less: Non-core investments	0.00	0.00	0.00	0.00	0.00
Invested capital	**27.42**	**28.17**	**30.65**	**25.21**	**21.00**
Fixed assets	0.02	0.01	0.01	0.00	0.00
Intangible assets	28.98	29.96	30.96	31.51	31.07
Capitalised R&D	0.00	0.00	0.00	0.00	0.00
Goodwill	0.00	0.00	0.00	0.00	0.00
Inventories	0.42	0.13	0.11	0.08	0.26
Trade debtors	*0.00*	*0.00*	*0.00*	*0.00*	*0.00*
Other debtors	*1.99*	*1.57*	*1.03*	*1.03*	*1.03*
Tax liability/credit	*0.00*	*0.00*	*1.50*	*3.36*	*1.32*
Trade creditors	*-1.49*	*-1.80*	*0.00*	*0.00*	*0.00*
Other creditors	*-2.50*	*-1.70*	*-2.95*	*-10.78*	*-12.68*
Debtors less creditors	-2.00	-1.93	-0.42	-6.39	-10.32
Invested capital	**27.42**	**28.17**	**30.65**	**25.21**	**21.00**
Net cash/(debt)	**20.98**	**13.30**	**9.78**	**6.02**	**0.83**

Source: Hardman & Co Life Sciences Research

Cashflow

- **General:** Given that STX outsources most of its operational activities, the cashflow statement is driven by the underling EBIT and licensing deals.
- **Norgine deal:** STX partnered with Norgine in Europe for Feraccru in 2018. On signing, STX received an upfront payment of £11m. Positive results from the head-to-head Feraccru study have triggered a €2.5m/£2.2m development milestone, included in 2019's 'other income'.
- **R&D spend:** STX retains considerable flexibility regarding its R&D investment into its next-generation products, the timing of which will be determined by the availability of appropriate resources. It is due to begin a Phase III trial in 2019.
- **US licensing deal:** All forecasts exclude potential 'other income', including from the licensing of Feraccru for the US market, the timing and quantum of which is difficult to predict. US 'other income' is likely to be considerably higher than that received from Norgine for European rights. Although some discussions are taking place, STX's expected strategy is to conclude a deal once the product has been fully de-risked by FDA approval.
- **Capital increase:** The capital increase in 2017 has provided sufficient funds to complete the AEGIS-H2H trial. However, given the scheduled paediatric study and potential outcomes studies, STX will likely require more funds in the future. This could come from one of, or a combination of, equity, debt and licensing/distribution deals.

Cashflow					
Year-end Dec (£m)	2016	2017	2018E	2019E	2020E
Underlying EBIT	-10.47	-18.34	-2.25	-6.75	-6.90
Depreciation	0.01	0.01	0.01	0.01	0.01
Amortisation	0.17	0.01	0.45	0.45	0.45
Inventories	*-0.42*	*0.29*	*0.02*	*0.03*	*-0.18*
Receivables	*-0.38*	*-0.17*	*0.54*	*0.00*	*0.00*
Payables	*-0.15*	*-0.41*	*-0.95*	*0.00*	*0.00*
Change in working capital	-0.95	-0.29	-0.40	0.03	-0.18
Exceptionals/provisions	0.10	0.10	0.14	0.14	0.14
Disposals	0.00	0.00	0.00	0.00	0.00
Other	0.18	0.00	0.00	0.00	0.00
Company operating cashflow	**-10.96**	**-18.10**	**-2.06**	**-6.13**	**-6.49**
Net interest	0.00	0.00	0.02	0.02	-0.03
Tax paid/received	0.00	1.99	1.86	3.36	1.32
Operational cashflow	**-10.96**	**-16.11**	**-0.18**	**-2.76**	**-5.19**
Capital expenditure	-0.01	0.00	0.00	0.00	0.00
Sale of fixed assets	0.00	0.00	0.00	0.00	0.00
Free cashflow	**-13.61**	**-19.29**	**-3.18**	**-3.76**	**-5.19**
Dividends	0.00	0.00	0.00	0.00	0.00
Acquisitions	-0.53	-0.24	-0.35	0.00	0.00
Disposals	0.00	0.00	0.00	0.00	0.00
Other investments	0.00	0.00	0.00	0.00	0.00
Cashflow after investments	**-14.13**	**-19.52**	**-3.53**	**-3.76**	**-5.19**
Share repurchases	-0.29	0.00	0.00	0.00	0.00
Share issues	33.51	11.88	0.00	0.00	0.00
Currency effect	0.98	0.00	0.00	0.00	0.00
Loans/cash acquired	0.18	0.00	0.00	0.00	0.00
Change in net debt	**20.25**	**-7.64**	**-3.53**	**-3.76**	**-5.19**
Hardman FCF/share (p)	-10.83	-14.34	-0.16	-2.35	-4.44
Opening net cash	0.7	21.0	13.3	9.8	6.1
Closing net cash	**21.0**	**13.3**	**9.8**	**6.1**	**0.9**

Source: Hardman & Co Life Sciences Research

Company matters

Registration

Incorporated in the UK with company registration number 09761509

Registered office:

Northern Design Centre
Baltic Business Quarter
Gateshead Quays
Newcastle
NE8 3DF

+44 (0) 191 511 8500

www.shieldtherapeutics.com

London office:

16 Upper Woburn Place
Euston
London
WC1H 0AF

+44 (0) 20 7186 8500

Board of Directors

Board of Directors

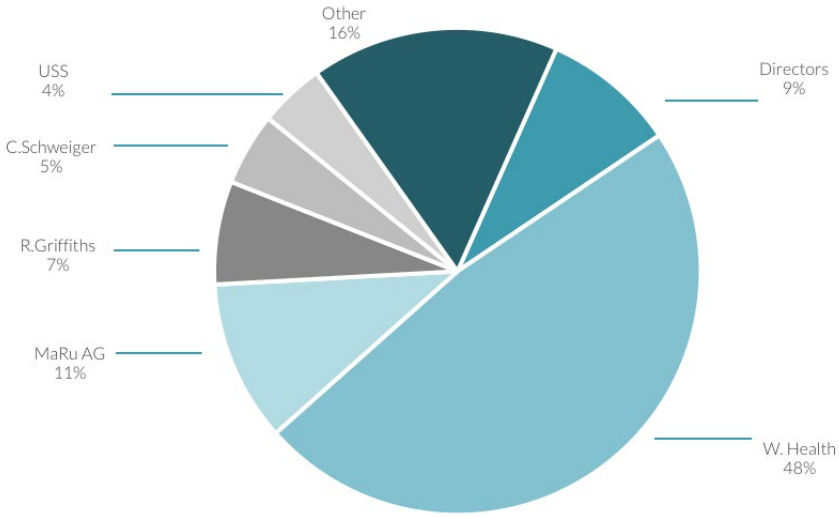
Position	Name	Nominations	Remuneration	Audit
Chairman	James Karis	M	M	
Founder and CEO	Carl Sterritt			
Non-executive director	Hans Peter Hasler	C		M
Non-executive director	Rolf Hoffmann	M	C	
Non-executive director	Peter Llewellyn-Davies	M		C

M = member; C = chair
Source: Company reports

Share capital

On 8 May 2019, there were 117,041,488 Ordinary shares in issue. In addition, there are 3.94m options outstanding.

Share register



Source: Hardman & Co Life Sciences Research

Sources

Bruck K *et al. CKD Prevalence Varies across the European General Population.* J Am Soc Nephrol. 2016;27(7):2135

Burisch J *et al. The burden of inflammatory bowel disease in Europe.* J Crohn's Colitis. 2013;7:322

Chrohn's & Colitis Foundation at http://www.crohnscolitisfoundation.org/

Centers for Disease Control and Prevention. *Chronic Kidney Disease Surveillance System—United States.* website. http://www.cdc.gov/ckd

El-Achkar T *et al. Higher prevalence of anemia with diabetes mellitus in moderate kidney insufficiency: The Kidney Early Evaluation Program.* 2005;67:1483

Fishbane S, Spinowitz B. *Update on Anemia in ESRD and Earlier Stages of CKD: Core Curriculum 2018.* Am J Kidney Dis. 2018;71(3):423

Harambat J *et al. Epidemiology of chronic kidney disease in children.* Pediatr Nephrol. 2012;27(3):363

Hill N *et al. Global prevalence of Chronic Kidney Disease – A systematic review and meta-analysis.* Plos One. 2016;11(7)

Kaitha *et al. Iron deficiency anemia in inflammatory bowel disease.* 2015;6(3):62

Rogler G, Vavricka S. *Anemia in inflammatory bowel disease: an under-estimated problem?* Front Med (Lausanne). 2015;1:58

Tulewicz-Marti E *et al. Management of anemia in inflammatory bowel disease; a challenge in everyday practice.* Prz Fasroenterol. 2017;12(4):239

Notes

Notes

Disclaimer

Hardman & Co provides professional independent research services and all information used in the publication of this report has been compiled from publicly available sources that are believed to be reliable. However, no guarantee, warranty or representation, express or implied, can be given by Hardman & Co as to the accuracy, adequacy or completeness of the information contained in this research and they are not responsible for any errors or omissions or results obtained from use of such information. Neither Hardman & Co, nor any affiliates, officers, directors or employees accept any liability or responsibility in respect of the information which is subject to change without notice and may only be correct at the stated date of their issue, except in the case of gross negligence, fraud or wilful misconduct. In no event will Hardman & Co, its affiliates or any such parties be liable to you for any direct, special, indirect, consequential, incidental damages or any other damages of any kind even if Hardman & Co has been advised of the possibility thereof.

This research has been prepared purely for information purposes, and nothing in this report should be construed as an offer, or the solicitation of an offer, to buy or sell any security, product, service or investment. The research reflects the objective views of the analyst(s) named on the front page and does not constitute investment advice. However, the companies or legal entities covered in this research may pay us a fixed fee in order for this research to be made available. A full list of companies or legal entities that have paid us for coverage within the past 12 months can be viewed at ducts . Hardman may provide other investment banking services to the companies or legal entities mentioned in this report.

Hardman & Co has a personal dealing policy which restricts staff and consultants' dealing in shares, bonds or other related instruments of companies or legal entities which pay Hardman & Co for any services, including research. No Hardman & Co staff, consultants or officers are employed or engaged by the companies or legal entities covered by this document in any capacity other than through Hardman & Co.

Hardman & Co does not buy or sell shares, either for their own account or for other parties and neither do they undertake investment business. We may provide investment banking services to corporate clients. Hardman & Co does not make recommendations. Accordingly, they do not publish records of their past recommendations. Where a Fair Value price is given in a research note, such as a DCF or peer comparison, this is the theoretical result of a study of a range of possible outcomes, and not a forecast of a likely share price. Hardman & Co may publish further notes on these securities, companies and legal entities but has no scheduled commitment and may cease to follow these securities, companies and legal entities without notice.

The information provided in this document is not intended for distribution to, or use by, any person or entity in any jurisdiction or country where such distribution or use would be contrary to law or regulation or which would subject Hardman & Co or its affiliates to any registration requirement within such jurisdiction or country.

Some or all alternative investments may not be suitable for certain investors. Investments in small and mid-cap corporations and foreign entities are speculative and involve a high degree of risk. An investor could lose all or a substantial amount of his or her investment. Investments may be leveraged and performance may be volatile; they may have high fees and expenses that reduce returns. Securities or legal entities mentioned in this document may not be suitable or appropriate for all investors. Where this document refers to a particular tax treatment, the tax treatment will depend on each investor's particular circumstances and may be subject to future change. Each investor's particular needs, investment objectives and financial situation were not taken into account in the preparation of this document and the material contained herein. Each investor must make his or her own independent decisions and obtain their own independent advice regarding any information, projects, securities, tax treatment or financial instruments mentioned herein. The fact that Hardman & Co has made available through this document various information constitutes neither a recommendation to enter into a particular transaction nor a representation that any financial instrument is suitable or appropriate for you. Each investor should consider whether an investment strategy of the purchase or sale of any product or security is appropriate for them in the light of their investment needs, objectives and financial circumstances.

This document constitutes a 'financial promotion' for the purposes of section 21 Financial Services and Markets Act 2000 (United Kingdom) ('FSMA') and accordingly has been approved by Capital Markets Strategy Ltd which is authorised and regulated by the Financial Conduct Authority (FCA).

No part of this document may be reproduced, stored in a retrieval system or transmitted in any form or by any means, mechanical, photocopying, recording or otherwise, without prior permission from Hardman & Co. By accepting this document, the recipient agrees to be bound by the limitations set out in this notice. This notice shall be governed and construed in accordance with English law. Hardman Research Ltd, trading as Hardman & Co, is an appointed representative of Capital Markets Strategy Ltd and is authorised and regulated by the FCA under registration number 600843. Hardman Research Ltd is registered at Companies House with number 8256259.

(Disclaimer Version 8 – Effective from August 2018)

Status of Hardman & Co's research under MiFID II

Some professional investors, who are subject to the new MiFID II rules from 3rd January, may be unclear about the status of Hardman & Co research and, specifically, whether it can be accepted without a commercial arrangement. Hardman & Co's research is paid for by the companies, legal entities and issuers about which we write and, as such, falls within the scope of 'minor non-monetary benefits', as defined in the Markets in Financial Instruments Directive II.

In particular, Article 12(3) of the Directive states: 'The following benefits shall qualify as acceptable minor non-monetary benefits only if they are: (b) 'written material from a third party that is commissioned and paid for by a corporate issuer or potential issuer to promote a new issuance by the company, or where the third party firm is contractually engaged and paid by the issuer to produce such material on an ongoing basis, provided that the relationship is clearly disclosed in the material and that the material is made available at the same time to any investment firms wishing to receive it or to the general public…'

The fact that Hardman & Co is commissioned to write the research is disclosed in the disclaimer, and the research is widely available.

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

In addition, it should be noted that MiFID II's main aim is to ensure transparency in the relationship between fund managers and brokers/suppliers, and eliminate what is termed 'inducement', whereby free research is provided to fund managers to encourage them to deal with the broker. Hardman & Co is not inducing the reader of our research to trade through us, since we do not deal in any security or legal entity.

research@hardmanandco.com

35 New Broad Street
London
EC2M 1NH

+44(0)20 7194 7622

www.hardmanandco.com