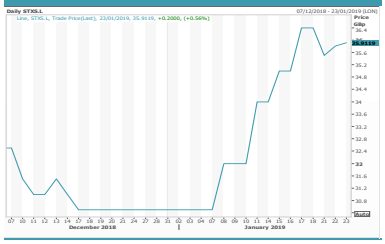
Pharmaceuticals & Biotechnology



Source: Eikon Thomson Reuters

Market data

EPIC/TKR	**STX**
Price (p)	**42.0**
12m High (p)	115.0
12m Low (p)	15.0
Shares (m)	116.4
Mkt Cap (£m)	48.9
EV (£m)	39.1
Free Float*	32%
Market	AIM

**As defined by AIM Rule 26*

Description

Shield Therapeutics (STX) is a commercial-stage pharmaceutical company delivering innovative specialty pharmaceuticals that address patients' unmet medical needs, with an initial focus on anemia 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	8.7%
W. Health	48.1%
MaRu AG	10.8%
R. Griffiths	7.8%
C. Schweiger	4.8%
USS	4.4%

Diary

1Q'19	AEGIS-H2H trial results
Apr-19	Finals
Jun-19	AGM
27-Jul	Feraccru PDUFA date

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SHIELD THERAPEUTICS

Cast-iron investment

Shield Therapeutics (STX) is a commercial-stage pharmaceutical company delivering specialty products that address patients' unmet medical needs in renal and gastrointestinal disorders. Its initial focus is Feraccru® a supplement for iron deficiency. Following IPO and EU approval of Feraccru, both in February 2016, STX has made good progress with its de-risked commercial strategy. Management has secured agreements with three partners with expertise in rare diseases and European market access to accelerate Feraccru's commercialisation. STX is now awaiting a game-changing FDA decision in 3Q'19 that could unlock the US market.

- **Strategy:** STX's strategy is to out-license the commercial rights to its products to expert partners for marketing and distribution 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 long-term commercial value.
- **Feraccru:** A novel treatment for iron deficiency (ID), Feraccru is approved for use across Europe in adults with or without anaemia. ID results from the depletion of iron stores in the liver, impacting production of red blood cells (which carry oxygen). Compared with other oral therapies, Feraccru is very well tolerated.
- **Coming up in 2019:** There are multiple potential inflection points ahead, not least the FDA approval decision, which would allow Feraccru to launch in the US. Nearer-term, results from the AEGIS-H2H (head-to-head) study will provide data to support reimbursement submissions in additional European markets.
- **Risks:** All drug companies carry development risk. However, STX has very limited risk because of the simplicity and low clinical risk of Feraccru, in addition to the fact that it has received regulatory approval in Europe and a decision date for US FDA approval. The main risk is, therefore, commercial execution.
- **Investment summary:** STX is at an interesting juncture. It has delivered on all goals set at the time of its IPO in 2016. Feraccru is a simple product, iron is essential for normal body function, and treatment fits easily into normal clinical practice. Validation by regulatory approval and commercial deals in Europe looks set to be repeated in the US. Given the potential news flow, a market capitalisation of just £49m makes STX a very interesting investment proposition.

Financial summary and valuation

Year-end Dec (£m)	2016	2017	2018E	2019E	2020E
Group sales	0.30	0.64	0.80	0.64	2.00
R&D	-2.03	-4.71	-4.30	-2.50	-2.50
Other income	0.04	0.00	11.10	0.00	0.00
EBITDA	-10.29	-17.95	-0.77	-6.25	-6.37
Underlying EBIT	-10.47	-18.38	-1.26	-6.74	-6.86
Reported EBIT	-12.46	-20.95	-3.73	-9.21	-9.33
Underlying PBT	-10.43	-18.38	-1.25	-6.73	-6.88
Statutory PBT	-15.60	-20.99	-3.72	-9.20	-9.35
Underlying EPS (p)	-9.73	-15.11	0.14	-4.71	-5.58
Statutory EPS (p)	-14.84	-17.43	-1.99	-7.52	-7.64
Net (debt)/cash	20.98	13.30	9.82	4.19	-1.23
Capital increase	33.51	11.88	0.00	0.00	0.00

Source: Hardman & Co Life Sciences Research

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Commercialisation underway

Simple product, large market

Introducing Shield Therapeutics…

…positive clinical and outcomes data…

…commercially validated

As growth-phase pharmaceutical companies go, STX is now a clinically and commercially de-risked proposition. Feraccru is a straightforward product with a very large potential market, and following approval in Europe in 2016, sales have increased each year. Its large potential market is driven by the ubiquity of iron deficiency (ID) worldwide and, as a supplement for chronic conditions, its repeated use. Feraccru's incorporation into NHS Trust policies and the recently signed commercial partnerships act as good validation of Feraccru's potential. In turn, STX has a semi-virtual business model, which allows an asset-light structure (and the associated flexibility and scalability), and a strategy to out-license its products for commercialisation.

This short report serves as an introduction to Hardman & Co's coverage of STX, providing background to Feraccru and describing its current commercialisation strategy. Our next note will provide further scientific background, full financial analysis, and a better understanding of STX's substantial valuation potential.

Iron deficiency (ID)

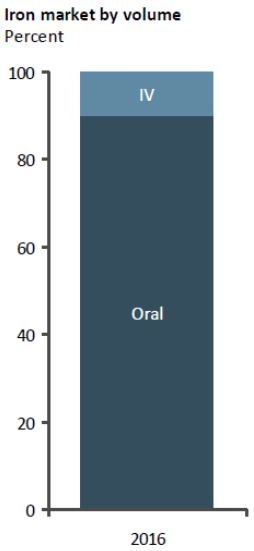
Iron is a low-risk product…

…that plays a vital role in normal body functioning

Iron is ubiquitous in the body and best known for its role in the synthesis of haemoglobin (Hb), which transports oxygen in red blood cells. It is stored in the liver and bone marrow, among other sites, and is released and sequestered among compartments in a highly dynamic process. When the body's requirement for iron exceeds its intake from food, iron stores are depleted, which can lead to ID. This ultimately affects the production of haemoglobin and red blood cells, resulting in fatigue and lethargy, the classic symptoms of anaemia. However, symptoms of ID are not specific and may develop slowly, so that they may not be readily recognised.

Prevalence and market

Iron supplement market



IV: intravenous
Source: Shield Therapeutics

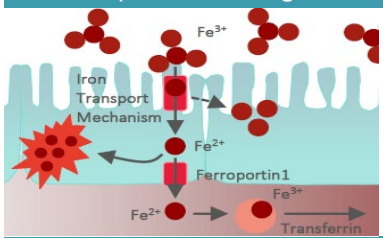
Anaemia is defined as am Hb level below 12g/dL in females and 13g/dL in males. Its most common cause worldwide is extreme ID, a condition in which there are no mobilisable iron stores and evidence of a compromised supply of iron to tissues. Anaemia is also associated with vitamin deficiencies (for example, vitamin C is required for iron absorption) and chronic conditions such as kidney disease, heart failure or inflammatory bowel disease (IBD). Feraccru was originally approved for use in adult IBD patients with iron deficiency anaemia (IDA), but in Europe, it is now indicated for all adult patients with ID, with or without anaemia.

ID has a global prevalence of 4%-12% in adults, with IDA affecting about half (2%-5%) of adult male and postmenopausal female patients. The WHO rates ID as the most common and widespread nutritional disorder in the world, and prevalence is expected to grow as aging populations drive an increase in chronic disorders. ID is treated through iron replacement therapy, using either oral products or intravenous (IV) administration. Although restoring iron levels more rapidly, IV iron is inconvenient and expensive, and must be administered in hospital due to the risk of iron overload and life-threatening hypersensitivity reactions. Salt-based oral therapies, on the other hand, are relatively cheap and accessible, but they are limited by poor tolerability in the gut and slower efficacy due to less efficient absorption.

Feraccru

Feraccru answers the tolerability issues of existing salt-based oral therapies on the basis of its chemical structure. Although not the focus of this short report, ferric maltol is a complex of Fe^{3+} and maltol molecules that remains soluble in the GI tract, only dissociating into maltol and iron when it is taken up by the cells lining the gut.

Iron transport in human gut



Source: Hardman & Co Life Sciences Research

The key point is that, unlike Feraccru, oral supplements that deliver iron in salt form require iron to dissociate from the carrier salt for uptake and can form insoluble products that collect and irritate the gut's lining. Moreover, since Fe^{3+} is a form that is accessible to the body's iron transport mechanism, its uptake is naturally regulated according to the body's needs, with any unabsorbed Feraccru excreted. Feraccru's capsule formulation makes it straightforward to administer, transport, and store.

De-risked and validated

Safe and effective in clinical studies

Feraccru has been shown to be safe and effective in four completed clinical trials, and it is being investigated in ongoing studies that are part of the product's reimbursement strategy and paediatric development plan associated with European and US approval. The original marketing authorisation in Europe was for adult IBD patients with IDA; the broader indication of adults with ID (with or without anaemia) was approved in Europe in February 2018. Trials are summarised in the table below.

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	Hb increase of 2.3g/dL within 12 weeks (p<0.0001)	Complete (late 2013)
	Adult IBD patients with IDA intolerant of other oral therapies	Excellent outcomes: 97% compliance levels	
	Placebo-controlled	Safe and no evidence of iron overload	
AEGIS-CKD	Pivotal trial submitted to FDA	Hb change of 0.6g/dL from baseline at 16 weeks.	Complete (March 2018)
	Adult CKD patients with IDA	Safe and no evidence of iron overload	
AEGIS-PAED	Phase I, pharmacokinetics study (dose finding)	Positive efficacy data – serum iron parameters met.	Complete (June 2018)
	Patients 12-17 years with ID	Good tolerance at all doses.	
AEGIS-H2H	Phase IIIb	Hb change from baseline at 12 weeks	Results expected 1Q'19
	Head-to-head comparison with IV ferric carboxymaltose		
	Adult IBD patients with IDA		
FRESH study	Real-world effectiveness of Feraccru in hospital practice		June 2018

CKD: Chronic Kidney Disease, Hb: haemoglobin, IV: intravenous,
Source: Hardman & Co Life Sciences Research

Third-party validation

Commercial 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 commercialisation partners signed in Europe. These partnerships provide early meaningful validation of the technology and its potential. Quarter-on-quarter sales growth has already been achieved, demonstrating demand for Feraccru.

The latest deal to be signed, in September 2018, is with Norgine, a European-focused speciality pharmaceuticals company. This grants Norgine an exclusive commercial licence to Feraccru in Europe (in territories not covered by STX's existing partners AOP and Ewopharma), Australia and New Zealand.

STX retains the IP and responsibility for the manufacture and supply of Feraccru, and all aspects of its development. The financial terms were as follows:

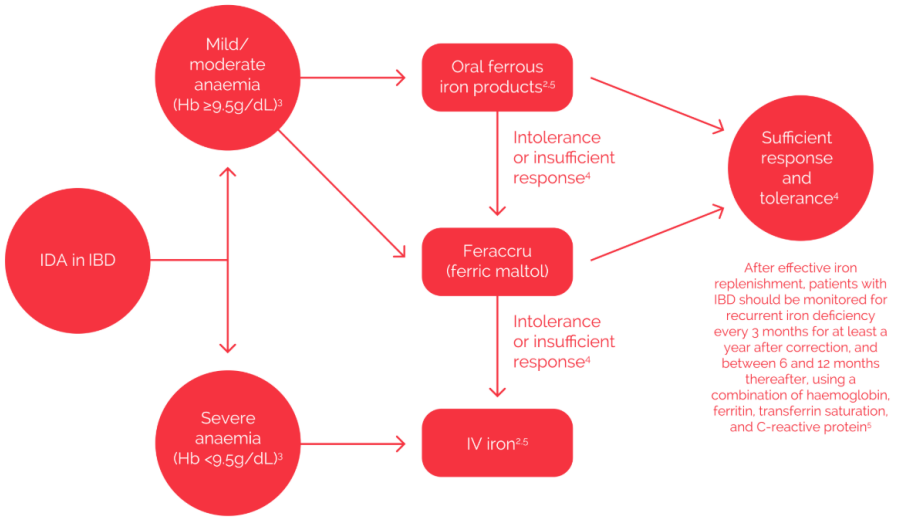
- £11m upfront licence payment to STX;
- a potential total of €54.5m in development and sales milestones; and
- tiered royalties of between 25% and 40% on Norgine's sales.

Payer validation

Clear, easily understood clinical pathway that fits with normal medical practice

Feraccru also has a strong cost-effectiveness profile, essential for accessing in full its target market. In England, it has been incorporated into multiple NHS Trust policies and hospital formularies, and it has achieved pricing and reimbursement agreements with clinical commissioning groups (CCGs). It has also been approved for reimbursement in Germany on a national basis.

Feraccru treatment pathway for IDA in IBD



Source: Shield Therapeutics

Additional real-world evidence, supporting full market access, was recently generated from the FRESH study involving seven UK hospitals. The results were very encouraging, being very similar to those of the controlled AEGIS-IBD study – 62% of patients had normalised Hb levels following treatment.

In terms of health economics data, a London NHS Trust health economics study suggested that treatment with Feraccru instead of iron infusions would save the Trust more than £250k, and more than 107 days of nursing time, on the basis of 800 patients treated each year.

Ongoing commercialisation strategy

Additional global launches

Feraccru launched in England and Germany in 2016 (where it is now commercialised by Norgine) and is in the reimbursement negotiation process for commercialisation in Switzerland. Because it is in the regulatory process for further European countries, additional launches can be expected in the near to medium term. Approvals in New Zealand and Australia are anticipated by 2020/2021, which will pave the way for launch by Norgine.

US strategy

The FDA decision day for Feraccru has been set for 27 July 2019

The big moment for Feraccru will be the FDA's approval decision, which has a PDUFA date (decision deadline) of 27 July this year. In line with its out-licensing strategy, STX's management has reiterated that a US launch is dependent on signing a commercial partner with US-specific expertise.

News flow

Operational progress and expected 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'19E	Preliminary results expected from AEGIS-H2H study	Compares Feraccru with IV iron: non-inferiority study
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

Investment summary

When STX was listed on AIM in February 2016, it raised £30.1m (net) of new capital at 150p a share, giving it a market capitalisation of £162m, to support the continuing investment in the clinical development of Feraccru and the initial phase of the product's commercial rollout. Even though management has delivered on its strategy to complete clinical trials to support the EU and US regulatory approvals of Feraccru, the stock has drifted down to a market cap of just £49m.

The STX investment proposition is very straightforward:

- a simple product containing iron, essential for normal body function, which addresses a clear unmet need in a highly prevalent disease;
- well understood science with very low risk;
- clear treatment pathway for Feraccru consistent with normal clinical practise;
- clear commercial strategy, validated by the Norgine partnership in the EU, which needs to be repeated in the US; and
- a strong balance sheet that supports modest cash burn, which could be boosted by R&D and sales milestones from Norgine and/or upfront payments from new commercial partners.

Financial summary

- At IPO in 2016, STX raised £32.5m gross (£30.1m net).
- During 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 on closing the deal.
- STX has an average monthly cash burn of £400k-£450k, influenced by the timing of clinical trial payments.
- No allowance has been made for R&D and sales milestones that may be received. A positive result in the upcoming AEGIS-H2H trial would trigger an estimated €2.5m receipt from Norgine.
- STX has a cash runway into 2020; however, this would be extended significantly by receipt of milestones, or of upfront payments from further commercial agreements.

Forecast summary

Year-end Dec (£m)	2016	2017	2018E	2019E	2020E	2021E
Profit & Loss						
Gross revenues	**0.3**	**0.6**	**11.9**	**0.6**	**2.0**	**6.7**
Sales	0.3	0.6	0.8	0.6	2.0	6.7
COGS	-0.1	-0.2	-0.4	-0.4	-1.2	-3.9
SG&A (underlying)	-8.7	-14.2	-8.5	-4.5	-5.2	-5.8
R&D	-2.0	-4.7	-4.3	-2.5	-2.5	-2.0
Other income	0.0	0.0	11.1	0.0	0.0	0.0
Underlying EBIT	**-10.5**	**-18.4**	**-1.3**	**-6.7**	**-6.9**	**-5.0**
Share-based costs	-0.3	-0.6	-0.5	-0.5	-0.5	-0.5
Exceptional items	-1.7	-2.0	-2.0	-2.0	-2.0	-2.0
Statutory EBIT	-12.5	-21.0	-3.7	-9.2	-9.3	-7.4
Net interest	0.0	0.0	0.0	0.0	0.0	0.0
Underlying pre-tax profit	**-10.4**	**-18.4**	**-1.3**	**-6.7**	**-6.9**	**-5.0**
Tax payable/credit	0.6	1.4	1.4	0.4	0.4	0.3
Weighted avg. shares (m)	101.2	112.4	116.4	116.4	116.4	116.4
Underlying basic EPS (p)	**-9.7**	**-15.1**	**0.1**	**-4.7**	**-5.6**	**-4.0**
Balance sheet @ 31 Dec						
Share capital	1.6	1.7	1.7	1.7	1.7	1.7
Reserves	46.8	39.5	37.1	28.4	19.5	12.4
Loans/overdrafts	0.0	0.0	0.0	0.0	0.0	0.0
less: Cash	21.0	13.3	9.8	4.2	-1.2	-5.8
Invested capital	**27.4**	**28.2**	**29.3**	**25.9**	**22.5**	**19.9**
Cashflow						
Underlying EBIT	-10.5	-18.4	-1.3	-6.7	-6.9	-5.0
Change in working capital	-0.9	-0.3	-0.4	0.3	-0.4	-1.9
Company op. cashflow	-11.0	-18.1	-1.1	-5.9	-6.7	-6.2
Capital expenditure	0.0	0.0	0.0	0.0	0.0	1.3
Acquisitions	-0.5	-0.2	-0.2	0.0	0.0	0.0
Share issues	33.5	11.9	0.0	0.0	0.0	0.1
Change in net debt	**20.2**	**-7.7**	**-3.5**	**-5.6**	**-5.4**	**-4.5**
Opening net cash	0.7	21.0	13.3	9.8	4.2	-1.2
Closing net cash	**21.0**	**13.3**	**9.8**	**4.2**	**-1.2**	**-5.8**

Source: Hardman & Co Life Sciences Research

Company matters

Registration

Incorporated in the UK with company registration number 09761509

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London office:

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WC1H 0AF

+44 (0) 20 7186 8500

Board of Directors

Board of Directors

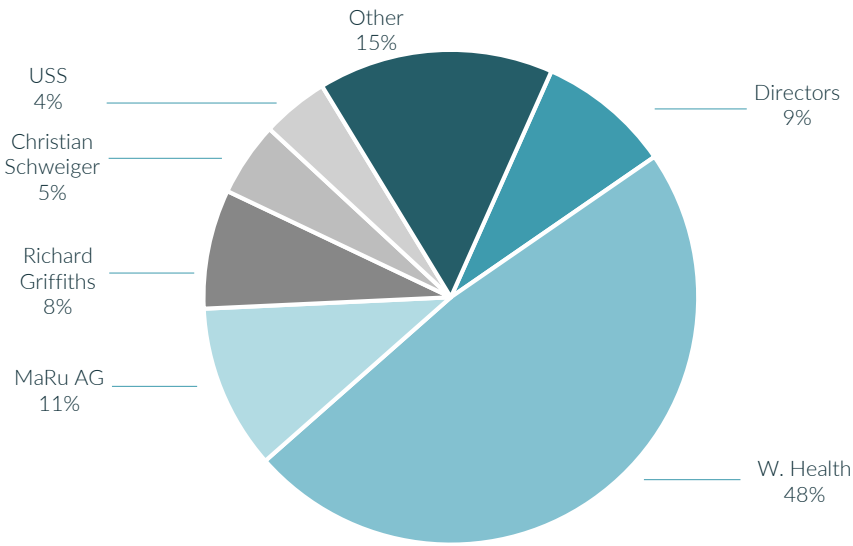
Position	Name	Nominations	Remuneration	Audit
Chairman	James Karis	M	M	
Founder and CEO	Carl Sterritt			
Non-executive director	Hans Peter Hasler	C		M
Non-executive director	Rolf Hoffmann	M	C	
Non-executive director	Peter Llewellyn-Davies	M		C

M = member; C = chair
Source: Company reports

Share capital

At 23 January 2019, there were 116,425,851 Ordinary shares in issue. In addition, there are 1.52m options outstanding.

Share register



Source: Hardman & Co Life Sciences Research

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