Pharmaceuticals & Biotechnology

Source: Refinitiv

Market data	
EPIC/TKR	**STX**
Price (p)	**182.5**
12m High (p)	202
12m Low (p)	28
Shares (m)	117.2
Mkt Cap (£m)	213.9
EV (£m)	204.2
Free Float*	33%
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	Tim Watts
Chairman	James Karis

+44 207 186 8500
www.shieldtherapeutics.com

Key shareholders

Directors	9.0%
W. Health	47.8%
MaRu AG	10.7%
R. Griffiths	6.8%
C. Schweiger	4.8%
USS	4.4%

Diary

4Q'19E	Accrufer deal
Apr'20	2019 final results
Mid-2020	Accrufer launch

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

More choice for clinicians and patients

Shield Therapeutics (STX) is a commercial-stage company delivering specialty products that address unmet medical needs, with an initial focus on treating iron deficiency (ID) with Feraccru®/Accrufer®. FDA approval of Accrufer with a broad label in the US opens up a market currently worth over $1bn in intravenous (IV) iron alone. Commercialisation of Feraccru is well under way in Europe, where it was approved in 2016; in the US, it is dependent on an upcoming licensing deal. Additional data released from the AEGIS head-to-head (H2H) study demonstrate favourable patient outcomes from Feraccru vs. IV iron treatment.

- **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 deals allow STX to retain its intellectual property (IP) and keep investing in its R&D pipeline, to benefit from both immediate and long-term value.
- **H2H data:** Top-line results demonstrating the non-inferiority of Feraccru to IV iron therapy were released in Mar'19. Additional information presented at a conference this week included the response rate for Feraccru, and its effectiveness in the maintenance of haemoglobin (Hb) levels.
- **More choice:** This is significant for patients and clinicians in providing an alternative option for treatment of IDA, particularly as an alternative to IV therapy in patients intolerant of other oral therapies. For payers like the NHS, Feraccru has cost-effectiveness benefits in preventing recurrence of IDA.
- **Risks:** All drug companies carry development risk. However, the risks with STX are limited because of Feraccru/Accrufer's simplicity and clinical profile. Given the FDA approval, the main risk is achieving the most appropriate commercial partner and executing on its global commercialisation strategy.
- **Investment summary:** The approval of Accrufer reinforces our view that STX is at an exciting juncture. It has delivered on all goals set at the time of its IPO in 2016. Feraccru/Accrufer has been validated by regulatory approval in both the EU and the US, and the commercial deal in Europe looks set to be repeated in the US. Announcement of its commercial partner, together with the terms of any deal, represent the next valuation inflection point.

Financial summary and valuation

Year-end Dec (£m)	2017	2018	2019E	2020E	2021E
Gross revenues	**0.64**	**11.88**	**2.93**	**2.15**	**3.15**
Sales	0.64	0.86	0.63	2.15	3.15
R&D	-4.71	-4.30	-3.31	-4.64	-3.89
Other income	0.00	11.03	2.30	0.00	0.00
EBITDA	-18.48	-2.47	-5.45	-9.19	-8.68
Underlying EBIT	-18.90	-3.26	-6.24	-9.98	-9.47
Reported EBIT	-20.95	-5.17	-8.15	-11.89	-11.38
Underlying PBT	-18.91	-3.26	-6.24	-10.02	-9.51
Statutory PBT	-20.99	-5.16	-8.14	-11.93	-11.42
Underlying EPS (p)	-15.58	0.09	-4.49	-7.96	-7.62
Statutory EPS (p)	-17.43	-1.55	-6.12	-9.58	-9.25
Net (debt)/cash	13.30	9.63	6.20	-1.27	-8.46

Source: Hardman & Co Life Sciences Research

More choice in IDA treatment

Additional data presented

Feraccru was non-inferior to IV iron in the AEGIS-H2H study…

…a well-controlled Phase 3b non-inferiority trial

The principal investigator on the study, Dr Stephanie Howaldt, presented results from the AEGIS-H2H trial at the United European Gastroenterology Week in a talk titled '*Oral Ferric Maltol vs. intravenous ferric carboxymaltose for the treatment of IDA in patients with in Irritable Bowel Disease (IBD): a multicentre phase 3b, open-label, randomised controlled trial*'. The key findings were:

- **Non-inferiority:** The mean response to Feraccru at 12 weeks was 74%, vs. 83% for IV iron. This was within the predefined margin and was statistically significant.
- **Recurrence prevented:** IDA recurred at least once in ca.39% (n=49) of IV arm patients (n=126) in the 52 weeks following initial IV iron treatment, but recurrence was prevented in the Feraccru arm patients (n=124).
- **Well tolerated:** Over 52 weeks, Feraccru's side-effect profile was consistent with that seen in previous studies, being well-tolerated even in patients unable to tolerate existing oral iron therapies.

Interpretation of AEGIS-H2H primary endpoint

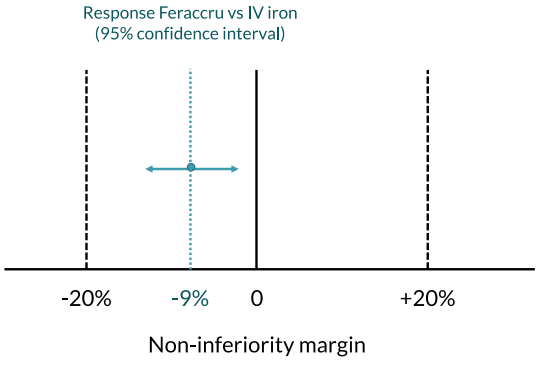
Feraccru has non-inferior efficacy to Ferinject…

…the IV iron market leader, which had global sales of $762m in 2018

The AEGIS-H2H was a non-inferiority trial, which is more complex to interpret than conventional superiority studies. To demonstrate Feraccru's positioning within the existing treatment pathway – as an alternative to IV iron in certain patients – STX needs evidence that Feraccru is not unacceptably less efficacious than IV iron. This was addressed by the primary endpoint of the H2H study.

The treatment response differed by 9% between Feraccru (mean response rate 74%) and IV iron (83%). As shown in the diagram below, the 95% confidence intervals around this 9% difference did not overlap the -20% margin or 0%, showing that Feraccru was not inferior to IV iron (and that it was also not superior). With an alpha of 2.5%, this was a statistically significant result (p=0.017).

Feraccru non-inferior to IV iron therapy



Source: Hardman & Co Life Sciences Research

Feraccru prevents recurrence of IDA

Furthermore, to gain reimbursement approval, STX and its partners (e.g. Norgine) need to show the incremental cost-effectiveness of Feraccru over IV iron. Although IV iron has a higher (but clinically similar) response rate, IV iron has the major disadvantage of having to be administered in the hospital/specialist clinic setting because of a risk, albeit low, of anaphylaxis. In addition, although existing salt-based oral therapies are cheap and accessible, their limitations are poor tolerability in the gut and slower efficacy due to less efficient absorption, particularly in irritable bowel

disease (IBD) patients. The secondary endpoint of the trial covered patient outcomes, which were shown to be favourable as follows:

- **Recurrence prevented:** IDA recurred at least once in ca.39% of IV arm patients in the year following initial treatment, but recurrence was prevented by Feraccru, with only a single patient in the Feraccru arm requiring intervention. This patient experienced an IBD flare, in which Feraccru is contraindicated along with other oral therapies due to absorption issues in the gut.
- **Prevents hospital visits:** The result of recurrence following IV iron therapy was 69 additional IV infusions, requiring costly and inconvenient ongoing hospital/clinic visits.
- **Tolerability:** IDA in IBD is particularly complex to treat, therefore the demonstration of Feraccru's tolerability over a long period in this patient population is very exciting for any patient with tolerability issues.

The immediate application of these results will be to strengthen the position of Norgine in negotiating pricing and reimbursement. Although Feraccru is launched in the UK and Germany, the major markets of Spain, Italy and France require reimbursement to be agreed prior to launch, and NICE in the UK has not yet provided recommendations.

Ferinject IV iron therapy

Source: Vifor Pharma UK

Treatment of IDA in IBD with Feraccru could save NHS more than £580,000…

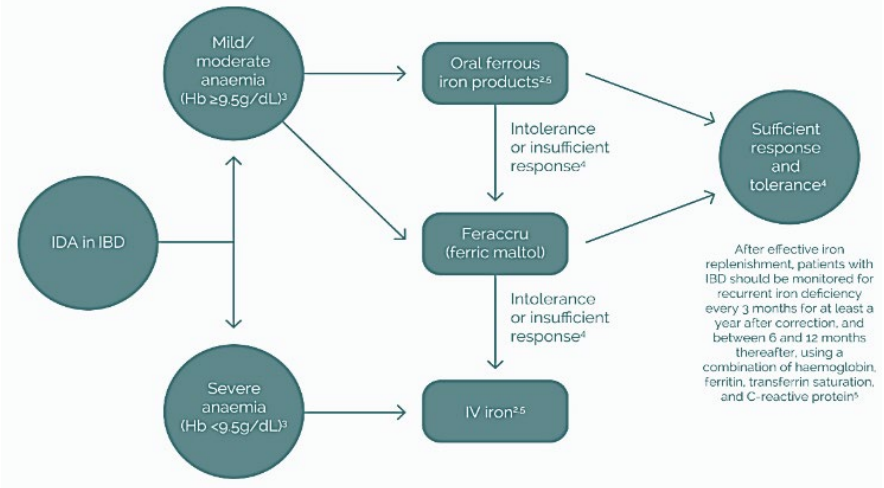
…compared with IV iron therapy treatment

As a guide, we estimate that treatment with Feraccru rather than IV iron could save the NHS more than £580,000 p.a. in treatment of IBD alone. Assuming it costs the NHS an additional £218[1] each time IDA recurrence is treated with IV iron rather than Feraccru, and assuming a similar recurrence rate in the IBD with IDA population in the UK as in the AEGIS-IBD trial, treatment of 74% of IBD with IDA patients with Feraccru, rather than IV iron, could result in a saving of at least £584,126 per year. A caveat to this analysis is that a relatively small proportion of IBD patients do tolerate oral iron salts, which are cheaper than both Feraccru and IV iron therapy.

More choice in treatment decisions

Overall, the main message from the AEGIS-H2H study is the added benefit to patients and an expanded choice for clinical decision making. Combined with prior studies, there is now a body of evidence showing that Feraccru can be used as an alternative to IV iron, particularly in patients who have not tolerated oral iron salts.

Iron deficiency treatment pathway



Source: Shield Therapeutics

[1] London Medicines Evaluation Network, 2016

Published data can now be used in promotional activities…

Importantly, now that the data have been officially peer-reviewed and 'published' at a scientific meeting, the results can be used in marketing materials and by Norgine's sales representatives in their activities promoting Feraccru. In the immediate term, this will apply to Germany and to areas of the UK where reimbursement is agreed with clinical commissioning groups (CCGs), which should directly result in an uptick in sales.

Investment conclusion

Valuation to be revisited on a US commercialisation deal…

As clinical adoption increases, it is likely that Feraccru may also be incorporated into the treatment pathway as a first-line alternative to treatment with existing oral iron salts, and potentially in treatment of general iron deficiency. We will continue to monitor progress, as this would greatly expand Feraccru's market. In addition, although the outcomes data from the AEGIS-H2H are unlikely to have so direct an effect on Accrufer pricing in the US, they do reduce the uncertainty surrounding the ability to achieve a higher list price now that it is approved.

FDA approval of Accrufer and minor adjustments to the model increased our sum-of-the-parts valuation for STX to £221m or 189p per share (from £194m/166p). A commercialisation deal with a US partner will be the next major inflection point, at which point we will upgrade our model to allow for the agreed deal terms.

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 http://www.hardmanandco.com/legals/research-disclosures. *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