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Shield Therapeutics plc
("Shield" or the "Group" or the "Company")

AEGIS-H2H study reanalysis demonstrates that
Feraccru®/Accrufer® is a credible alternative to IV therapy for iron deficiency anaemia

Feraccru®/Accrufer® corrects anaemia and maintains Hb levels over the long term

London, UK, 6 August 2020: Shield Therapeutics plc (LSE: STX), a commercial stage, pharmaceutical company with a focus on addressing iron deficiency with its lead product Feraccru®/Accrufer® (ferric maltol), provides the headline results from the reanalysis of the AEGIS-H2H study.

The AEGIS-H2H study was intended and designed to provide data comparing oral Feraccru®/Accrufer® against intravenous (IV) iron therapy from which health economics data and other analysis could be generated. The study was not intended as a registration study and the regulatory status of Feraccru®/Accrufer® is unaffected by the study. On 17 March 2020 Shield announced an update and clarification relating to the original results of the AEGIS-H2H study (announced in March 2019) and that the Board had instigated a thorough and complete review into the analysis. This review has now been completed, including an independent statistical review.

The Feraccru®/Accrufer® AEGIS-H2H study was a multi-national Phase IIIb randomised study in 250 inflammatory bowel disease (IBD) patients with mild to severe iron deficiency anaemia (IDA) and baseline haemoglobin (Hb) measurements at the start of the study as low as 8.0g/dL. The main objectives of the study were to compare the impact of Feraccru®/Accrufer® on Hb levels over 52 weeks with that of Ferinject® (ferric carboxymaltose (FCM)), the market-leading intravenously (IV) delivered iron replacement therapy treatment. Patients were monitored 5 times during the course of the study, at weeks 4, 12, 24, 36 and 52. Reflecting clinical practice, IV FCM was administered in the study according to each physician's local prescribing information which allow, in some participating countries, for multiple additional IV dosing whereas Feraccru®/Accrufer® could only be given 30 mg twice daily in line with the US and European approved label.

The first 12-week phase compared the initial Hb response in patients, with a "response" defined for the purpose of the primary endpoint as the normalisation of Hb levels or an increase of at least 2g/dL in Hb from patients' baseline levels. The primary endpoint of the study was defined as achieving non-inferiority in the proportion of responders in both the "intention to treat" (ITT)[(1)] and "per protocol" (PP)[(1)] populations at the end of the initial 12 weeks. The March 2020 RNS clarified that the study had not met this 12-week primary endpoint. The initial 12-week period was followed by a 40-week extension phase, during which patients continued treatment with Feraccru®/Accrufer® or received further IV iron infusions in line with clinical need. The purpose of this second phase was to understand how well each therapy maintained Hb levels and corrected anaemia and to enable evaluations of health economic outcomes. For health economics analysis, the ITT population is preferred as this is considered to be closer to real world experience than the PP population.

The headline results from the reanalysis of the data are as follows:

By week 12 (first phase)

- Of the patients treated with Feraccru®/Accrufer®, 67% of the ITT population and 68% of the PP population had responded to treatment as defined above. In the IV arm, 84% of the ITT population and 85% of the PP population had responded meaning that Feraccru®/Accrufer® did not achieve non-inferiority at 12 weeks in the primary endpoint in either population.
- The mean increase in Hb levels per patient in the Feraccru®/Accrufer® arm was clinically significant at 2.45 g/dL for the ITT population and 2.57 g/dL in the PP population, compared with 3.04 g/dL and 3.05 g/dL respectively for IV-treated patients.

Long term phase (using the ITT results)

- By week 24, 65% Feraccru®/Accrufer® of those patients still being monitored had achieved normal levels of Hb[(2)] and therefore were non-anaemic, compared with 68% of IV patients.
- At weeks 24, 36 and 52, the mean increases in Hb levels in those patients still being monitored were 2.93 g/dL, 3.16 g/dL and 2.72 g/dL in the Feraccru®/Accrufer® arm compared with 2.84 g/dL, 2.70 g/dL and 2.79 g/dL in the IV arm.

Health economics benefits

During the first 12-week phase of the study, 82% of IV patients received more than one infusion and collectively 138 days were taken off work in this phase. In the extension phase from week 13 to week 52, 47% of patients who were monitored after the week 12 visit required at least one further infusion. The health economic outcomes from these results, and other more detailed results from the study, are broadly unchanged from the original 2019 analysis and demonstrate that Feraccru®/Accrufer® compares favourably with IV therapy. For example, in an abstract[(3)] published at the European Crohn's and Colitis Organisation (ECCO) congress in February 2020, the authors concluded that the *"mean total per-patient drug costs (acquisition + administration) were approximately 1.6 times higher for treatment with IV FCM than ferric maltol, when modelled for a German healthcare setting. The higher cost of IV FCM is driven by higher drug cost and costs of IV administration. As an oral treatment ferric maltol has no administration-related costs or resource use, thus reducing the burden on payers and local health care services."*

Shield plans to publish the full AEGIS-H2H study results in a peer-reviewed paper in due course.

Dr Stephanie Howaldt, one of the study investigators and a co-author of the ECCO abstract, commented on the reanalysis of these results, saying: "*In my daily clinical practice, I am looking for an effective, easy to use, well tolerated and cost-efficient long-term therapeutic approach treating patients with IDA. This analysis showed clinical meaningful responses with both ferric carboxymaltose and ferric maltol after 4 weeks and the results are consistent with the ferric maltol pivotal Phase III study programme. Most importantly, ferric maltol demonstrated comparable effectiveness at maintaining Hb and iron status for up to 52 weeks, preventing relapse, which was seen frequently in the ferric carboxymaltose group, requiring additional IV therapy. Ferric maltol is therefore an appropriate cost-effective alternative to IV iron especially for long-term treatment of IDA in IBD.*"

Tim Watts, CEO of Shield Therapeutics also commented, saying: *"We are very pleased that the reanalysis of the AEGIS-H2H study data demonstrates that Feraccru®/Accrufer® is a credible alternative to IV therapy and offers economic advantages. Having resolved the anomalies seen in the original analysis the study results can now be used with confidence for further health economics analysis and to support pricing and reimbursement applications in Europe."*

Note 1 – The ITT population refers to all patients who were randomised into the study, whether or not they completed the study in compliance with the study design. The PP population includes only those patients who completed each phase of the study in accordance with the study design.

Note 2 – Normal levels of Hb are defined by the World Health Organisation as 12 g/dL for women and 13 g/dL for men

Note 3 - ECCO abstract EC20-0754 "Health care resource use associated with ferric maltol and IV iron treatment for iron deficiency anaemia in patients with Inflammatory Bowel Disease" https://www.ecco-ibd.eu/publications/congress-abstracts/item/p685-healthcare-resource-use-associated-with-ferric-maltol-and-iv-iron-treatment-for-iron-deficiency-anaemia-in-patients-with-inflammatory-bowel-disease.html

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About Shield Therapeutics plc

Shield is a de-risked, specialty pharmaceutical company focused on commercialising its lead product, Feraccru®/Accrufer®, a novel, stable, non-salt based oral therapy for adults with iron deficiency with or without anaemia. Feraccru®/Accrufer® has been approved for use in the United States, European Union, UK and Switzerland and has exclusive IP rights until the mid-2030s. Feraccru is commercialised in the UK and Europe by Norgine B.V. and the Company is currently in the process of selecting a commercialisation partner for the US market. Shield also has an exclusive licence agreement with Beijing Aosaikang Pharmaceutical Co., Ltd., for the development and commercialisation of Feraccru®/Accrufer® in China, Hong Kong, Macau and Taiwan.

For more information, please visit www.shieldtherapeutics.com. Follow Shield on Twitter @ShieldTx