GSK reports outcome from US FDA Advisory Committee meeting on daprodustat for anaemia of CKD

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For media and investors only

GSK plc (LSE/NYSE: GSK) today reports that the US Food and Drug Administration (FDA) Cardiovascular and Renal Drugs Advisory Committee (CRDAC) supported that the benefit of treatment with daprodustat outweighs the risks for adult dialysis patients with anaemia of chronic kidney disease (CKD) with a 13 to 3 vote. In adult non-dialysis patients with anaemia of CKD, the CRDAC did not support that the benefit of treatment with daprodustat outweighs the risks with a 5 to 11 vote.

The US FDA will consider the vote, feedback, and recommendations from the CRDAC as it reviews the New Drug Application (NDA) and is not bound by the Committee's recommendation. The CRDAC provides the US FDA with independent, expert advice and reviews and evaluates available data concerning the safety and efficacy of marketed and potential new medicines for use in the treatment of cardiovascular and renal disorders. In April 2022, the US FDA accepted the NDA for daprodustat and assigned a Prescription Drug User Fee Act date of 1 February 2023.

CKD is an increasing global health burden affecting 700 million patients worldwide, with an estimated one in seven patients also developing anaemia, resulting in increased morbidity, mortality and reduced quality of life. When not adequately managed in certain patients, it can result in exhaustion and limit the ability to function in day-to-day life. When left untreated or undertreated, anaemia of CKD is associated with poor clinical outcomes and leads to a substantial burden on patients and healthcare systems. There remains an unmet need for convenient treatment options with efficacy and safety

comparable to current treatments.

Chris Corsico, Senior Vice President, Development, GSK, said:

> Today's robust discussion was an important step in the review of daprodustat. We are pleased the committee recognised the potential for daprodustat to help certain patients who are living with anaemia of CKD given limited treatment options. We want to thank the physicians, patients and advocacy community who shared their valuable insights about this disease. We look forward to continuing to work with the US FDA as they complete their review of our new drug application.

Daprodustat, an oral hypoxia-inducible factor prolyl hydroxylase inhibitor (HIF-PHI), was studied in the ASCEND phase III clinical trial programme, which included five pivotal trials assessing the efficacy and safety of daprodustat for the treatment of anaemia across the spectrum of CKD. All five pivotal trials met the primary endpoints. Results from two trials were published in the New England Journal of Medicine in November 2021, which included non-dialysis (ASCEND-ND) and dialysis (ASCEND-D) CKD patients. Additional results were also published in the New England Journal of Medicine supplementary appendix, which included non-dialysis (ASCEND-ND) and dialysis (ASCEND-D) CKD patients.

In March 2022, the European Medicines Agency validated the marketing authorisation application for daprodustat, which is currently under regulatory review, with a regulatory decision anticipated in the first half of 2023. In June 2020, Duvroq (daprodustat) tablets were approved by Japan's Ministry of Health, Labour and Welfare for the treatment of patients with anaemia of CKD. Duvroq is the market leader and preferred HIF-PHI in Japan.

About the ASCEND phase III clinical trial programme

The ASCEND programme includes five phase III trials to assess the efficacy and safety profile of daprodustat for the treatment of anaemia of CKD across the disease spectrum. The programme enrolled over 8,000 patients treated for up to 4.26 years. Results from all five trials were presented at the American Society of Nephrology's Kidney Week 2021.

Results from the two pivotal cardiovascular outcomes studies,

ASCEND-ND and ASCEND-D, which investigated patients not on dialysis and on dialysis, respectively, were also published in the New England Journal of Medicine,:

ASCEND-ND(Anaemia Studies in CKD: Erythropoiesis via a Novel PHI Daprodustat-Non-Dialysis) enrolled 3,872 non-dialysis dependent patients with anaemia of CKD who were either switched from the standard of care (ESA) or not currently receiving ESA therapy to receive daprodustat or ESA control (darbepoetin alfa). Iron management protocols were instituted across both arms of the trial. The trial met its primary efficacy and safety endpoints. Results showed that daprodustat improved and/or maintained haemoglobin (Hb) within the target level (10-11.5 g/dL) for these patients, and the primary safety analysis of the intention-to-treat (ITT) population showed that daprodustat achieved non-inferiority of major adverse cardiovascular events (MACE) compared to ESA control.

ASCEND-D(Anaemia Studies in CKD: Erythropoiesis via a Novel PHI Daprodustat-Dialysis) enrolled 2,964 dialysis patients with anaemia of CKD who were switched to receive daprodustat or ESA control from a standard of care ESA therapy. A uniform iron management protocol was instituted across both arms of the trial. The trial met its primary efficacy and safety endpoints. Results showed that daprodustat improved or maintained Hb within target levels (10-11.5 g/dL) for these patients, and the primary safety analysis of the ITT population showed that daprodustat achieved non-inferiority of MACE compared to ESA control.

Additional results were also published in the New England Journal of Medicine supplementary appendix, which included non-dialysis (ASCEND-ND) and dialysis (ASCEND-D) CKD patients.

About anaemia of chronic kidney disease

CKD, characterised by progressive loss of kidney function, is an increasing global public health burden. Risk factors for CKD include hypertension, diabetes, obesity and primary renal disorders.iii Furthermore, CKD is an independent risk factor for cardiovascular disease.iii Anaemia is an important and frequent complication of CKD. However, it is often poorly diagnosed and undertreated in patients with early-stage CKD, such as those not on dialysis.iv Over 700 million patients suffer from CKD worldwide, and an estimated one in seven have anaemia., When left untreated or undertreated, anaemia

of CKD is associated with poor clinical outcomes and leads to a substantial burden on patients and healthcare systems.iv

Daprodustat, a HIF-PHI, belongs to a novel class of oral medicines being studied for the treatment of anaemia of CKD in adult patients not on dialysis and on dialysis. Inhibition of oxygen-sensing prolyl hydroxylase enzymes stabilises hypoxia-inducible factors, which can lead to transcription of erythropoietin and other genes involved in the correction of anaemia, similar to the physiological effects that occur in the human body at high altitude. Daprodustat is being developed to provide a convenient oral treatment option for patients with anaemia of CKD.

GSK is a global biopharma company with a purpose to unite science, technology, and talent to get ahead of disease together. Find out more at gsk.com/company.

Cautionary statement regarding forward-looking statements

GSK cautions investors that any forward-looking statements or projections made by GSK, including those made in this announcement, are subject to risks and uncertainties that may cause actual results to differ materially from those projected. Such factors include, but are not limited to, those described in the Company's Annual Report on Form 20-F for 2021, GSK's Q2 Results for 2022 and any impacts of the COVID-19 pandemic.

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