US FDA accepts new drug application for GSK's momelotinib for the treatment of myelofibrosis

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For media and investors only

- Regulatory submission included data from the pivotal MOMENTUM phase III clinical trial that met all primary and key secondary efficacy endpoints

GSK plc (LSE/NYSE: GSK) today announced that the US Food and Drug Administration (FDA) accepted the New Drug Application (NDA) for momelotinib, a potential new medicine with a proposed differentiated mechanism of action that may address the significant unmet medical needs of myelofibrosis patients with anaemia. The US FDA has assigned a Prescription Drug User Fee Act action date of 16 June 2023.

The NDA is based on the results from key phase III trials, including the pivotal MOMENTUM trial, which met all primary and key secondary endpoints, including Total Symptom Score (TSS), Transfusion Independence (TI) rate and Splenic Response Rate (SRR). The primary analysis data from the MOMENTUM trial were recently presented at the 2022 American Society of Clinical Oncology Annual Meeting and the European Hematology Association 2022 Hybrid Congress.

Momelotinib is not currently approved in any market.

About the pivotal MOMENTUM phase III clinical trial

MOMENTUM is a global, randomised, double-blind phase III clinical trial of momelotinib versus danazol in patients with myelofibrosis who were symptomatic and anaemic and had been previously treated with an FDA-approved JAK inhibitor. The trial was designed to evaluate the

safety and efficacy of momelotinib for treating and reducing key hallmarks of the disease: symptoms, blood transfusions (due to anaemia) and splenomegaly (enlarged spleen).

The trial's primary efficacy endpoint was TSS reduction of ≥50% over the 28 days immediately before the end of Week 24 compared to baseline TSS, using the Myelofibrosis Symptom Assessment Form. Key secondary endpoints included TI rate for ≥12 weeks immediately before the end of Week 24 with haemoglobin levels ≥ 8 g/dL and SRR based on splenic volume reduction of ≥35% at Week 24 from baseline.

Patients were randomised at 2:1 to receive either momelotinib or danazol (n=130 and n=65, respectively). After 24 weeks of treatment, patients on danazol were allowed to crossover to receive momelotinib. Early crossover to momelotinib was available for confirmed splenic progression. The trial enrolled 195 patients across 21 countries.

Momelotinib is a potential new medicine with a differentiated mechanism of action, with inhibitory ability along three key signalling pathways: Janus kinase (JAK) 1, and JAK2 and activin A receptor, type I (ACVR1). 1, 2, 3, 4 Inhibition of JAK1 and JAK2 may improve constitutional symptoms and splenomegaly. 1, 2, 4 Additionally, direct inhibition of ACVR1 leads to a decrease in circulating hepcidin, which is elevated in myelofibrosis and contributes to anaemia. 1, 2, 3, 4

Momelotinib was most recently developed by Sierra Oncology, Inc., which GSK acquired in July 2022, building on GSK’s expertise in haematology and portfolio of specialty medicines and vaccines.

Myelofibrosis is a rare blood cancer that results from dysregulated JAK-signal transducer and activator of transcription protein signalling and is characterised by constitutional symptoms, splenomegaly, and progressive anaemia. Myelofibrosis affects approximately 20,000 patients in the US, with about 40% of patients already anaemic at the time of diagnosis and nearly all patients estimated to develop anaemia eventually. 1, 5 Patients will often require transfusions, and more than 30% will discontinue treatment due to anaemia. 6 Anaemia and transfusion dependence strongly correlate with poor prognosis and shortened survival. 7

GSK is focused on maximising patient survival through transformational medicines. GSK’s pipeline is focused on immuno-oncology, cell therapy, tumour cell targeting therapies and synthetic

lethality. Our goal is to achieve a sustainable flow of new treatments based on a diversified portfolio of investigational medicines utilising modalities such as small molecules, antibodies, antibody-drug conjugates, and cell therapy, either alone or in combination.

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

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6 Palandri, F., Palumbo, G.A., Elli, E.M. et al. Ruxolitinib discontinuation syndrome: incidence, risk factors, and management in 251 patients with myelofibrosis. Blood Cancer J. 11, 4 (2021). https://doi.org/10.1038/s41408-020-00392-1

7 Pardanani, A., & Tefferi, A. (2011). Prognostic relevance of anemia and transfusion dependency in myelodysplastic syndromes and primary myelofibrosis. Haematologica, 96(1), 8–10. https://doi.org/10.3324/haematol.2010.035519

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