GSK

Stock-exchange announcement

For media and investors only

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Ojjaara (momelotinib) approved in the US as the first and only treatment indicated for myelofibrosis patients with anemia

- Approval is for use in myelofibrosis patients with anemia regardless of prior myelofibrosis therapy
- Nearly all myelofibrosis patients are estimated to develop anemia over the course of the disease, and over 30% will discontinue treatment due to anemia[1,2,3]
- *Ojjaara* addresses key manifestations of myelofibrosis, namely anemia, constitutional symptoms and splenomegaly

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GSK plc (LSE/NYSE: GSK) today announced that the US Food and Drug Administration (FDA) has approved *Ojjaara* (momelotinib) for the treatment of intermediate or high-risk myelofibrosis, including primary myelofibrosis or secondary myelofibrosis (post-polycythemia vera and post-essential thrombocythemia), in adults with anemia. *Ojjaara* is a once-a-day, oral JAK1/JAK2 and activin A receptor type 1 (ACVR1) inhibitor. To date, it is the only approved medicine for both newly diagnosed and previously treated myelofibrosis patients with anemia that addresses the key manifestations of the disease, namely anemia, constitutional symptoms, and splenomegaly (enlarged spleen).[4]

Nina Mojas, Senior Vice President, Oncology Global Product Strategy, GSK, said: "The vast majority of myelofibrosis patients eventually develop anemia, causing them to discontinue treatments and require transfusions. Given this high unmet need, we are proud to add *Ojjaara* to our oncology portfolio and address a significant medical need in the community. We look forward to helping improve outcomes in this difficult-to-treat blood cancer."

Myelofibrosis is a blood cancer affecting approximately 25,000 patients in the US.[4,5,6] Myelofibrosis can lead to severely low blood counts, including anemia and thrombocytopenia; constitutional symptoms such as fatigue, night sweats, and bone pain; and splenomegaly. About 40% of patients have moderate to severe anemia at the time of diagnosis, and nearly all patients are estimated to develop anemia over the course of the disease.[7,8,9,10] Physicians have had limited treatment options to treat myelofibrosis patients with anemia. These patients often require transfusions and more than 30% will discontinue treatment due to anemia.[3] Patients who are transfusion dependent have a poor prognosis and shortened survival.[1,11,12,13,14,15,16,17,18]

Ruben A. Mesa, MD, FACP, President and Executive Director, Atrium Health Levine Cancer Center and Atrium Health Wake Forest Baptist Comprehensive Cancer Center, said: "With momelotinib we have the potential to establish a new standard of care for myelofibrosis patients with anemia. Addressing key manifestations of myelofibrosis, including anemia, constitutional symptoms and splenomegaly, makes a significant difference in the treatment regimen for these patients who have limited options to address these aspects of the disease."

The FDA approval of momelotinib is supported by data from the pivotal MOMENTUM study and a subpopulation of adult patients with anemia from the SIMPLIFY-1 phase III trial. MOMENTUM was designed to evaluate the safety and efficacy of momelotinib versus danazol for the treatment and reduction of key manifestations of myelofibrosis in an anemic, symptomatic, JAK inhibitor-experienced population. The MOMENTUM trial met all its primary and key secondary endpoints, demonstrating statistically significant response with respect to constitutional symptoms, splenic response and transfusion independence, in patients treated with momelotinib versus danazol.[2] SIMPLIFY-1 was designed to evaluate the efficacy and safety of momelotinib versus ruxolitinib in myelofibrosis patients who

had not received a prior JAK-inhibitor therapy.[1] Safety and efficacy results for SIMPLIFY-1 were based upon a subset of patients with anemia.

In these clinical trials, the most common adverse reactions were thrombocytopenia, hemorrhage, bacterial infection, fatigue, dizziness, diarrhea, and nausea.[19]

Kapila Viges, Chief Executive Officer, MPN (Myeloproliferative Neoplasms) Research Foundation, said: "We are thrilled to see momelotinib reach the clinic, giving patients and their physicians another option to help manage myelofibrosis. Any new treatment that takes steps toward unlocking the mysteries of this complex and chronic blood cancer represents great progress for the field."

Momelotinib is currently not approved in any other market.

About myelofibrosis
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 anemia. Myelofibrosis affects approximately 25,000 patients in the US.[1,5,6]

About the pivotal MOMENTUM clinical trial
MOMENTUM was a phase III, global, multicenter, randomized, double-blind study investigating momelotinib versus danazol in patients with myelofibrosis who were symptomatic and anemic and had been previously treated with an 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 anemia) and splenomegaly.[2] Results from the 24-week treatment period were presented at the 2022 American Society of Clinical Oncology (ASCO) Annual Meeting and subsequently published in *The Lancet*.[20,21]

About the SIMPLIFY-1 clinical trial
SIMPLIFY-1 was a multicenter, randomized, double-blind, phase III study that compared the safety and efficacy of momelotinib to ruxolitinib in patients with myelofibrosis who had not received prior treatment with a JAK inhibitor. Safety and efficacy results for SIMPLIFY-1 were based upon a subset of patients with anemia (haemoglobin <10 g/dL) at baseline. The efficacy of momelotinib in the treatment of patients with myelofibrosis in SIMPLIFY-1 was based on spleen volume response (reduction by 35% or greater).

About *Ojjaara* (momelotinib)
Ojjaara has a differentiated mechanism of action, with inhibitory ability along three key signalling pathways: Janus kinase (JAK) 1, JAK2, and activin A receptor, type I (ACVR1).[2,6,22,23] Inhibition of JAK1 and JAK2 may improve constitutional symptoms and splenomegaly.[2,6,23] Additionally, inhibition of ACVR1 leads to a decrease in circulating hepcidin, which is elevated in myelofibrosis and contributes to anemia.[2,6,22,23]

INDICATION
OJJAARA is indicated for the treatment of intermediate or high-risk myelofibrosis (MF), including primary MF or secondary MF [post-polycythemia vera (PV) and post-essential thrombocythemia (ET)], in adults with anemia.

IMPORTANT SAFETY INFORMATION
Risk of Infections

- Serious (including fatal) infections (e.g., bacterial and viral, including COVID-19) occurred in 13% of patients treated with OJJAARA. Infections regardless of grade occurred in 38% of patients. Delay starting therapy until active infections have resolved. Monitor patients for signs and symptoms of infection and initiate appropriate treatment promptly.

Hepatitis B Reactivation

- Hepatitis B viral load (HBV-DNA titer) increases, with or without associated elevations in alanine transaminase (ALT) or aspartate transaminase (AST), have been reported in patients with chronic hepatitis B virus (HBV) infection taking Janus Kinase (JAK) inhibitors, including OJJAARA. The effect of OJJAARA on viral replication in patients with chronic HBV infection is unknown. In patients with HBV infections, check

hepatitis B serologies prior to starting OJJAARA. If HBsAg and/or anti-HBc antibody is positive, consider consultation with a hepatologist regarding monitoring for reactivation versus prophylactic hepatitis B therapy. Patients with chronic HBV infection who receive OJJAARA should have their chronic HBV infection treated and monitored according to clinical HBV guidelines.

Thrombocytopenia and Neutropenia

- New or worsening thrombocytopenia, with platelet count less than 50 × 10^9/L, was observed in 20% of patients treated with OJJAARA. Eight percent of patients had baseline platelet counts less than 50 × 10^9/L.
- Severe neutropenia, absolute neutrophil count (ANC) less than 0.5 × 10^9/L, was observed in 2% of patients treated with OJJAARA.
- Assess complete blood counts (CBC), including platelet and neutrophil counts, before initiating treatment and periodically during treatment as clinically indicated. Interrupt dosing or reduce the dose for thrombocytopenia or neutropenia.

Hepatotoxicity

- Two of the 993 patients with MF who received at least one dose of OJJAARA in clinical trials experienced reversible drug-induced liver injury. Overall, new or worsening elevations of ALT and AST (all grades) occurred in 23% and 24%, respectively, of patients treated with OJJAARA; Grade 3 and 4 transaminase elevations occurred in 1% and 0.5% of patients, respectively. New or worsening elevations of total bilirubin occurred in 16% of patients treated with OJJAARA. All total bilirubin elevations were Grades 1-2. The median time to onset of any grade transaminase elevation was 2 months, with 75% of cases occurring within 4 months.
- Delay starting therapy in patients presenting with uncontrolled acute and chronic liver disease until apparent causes have been investigated and treated as clinically indicated. When initiating OJJAARA, refer to dosing in patients with hepatic impairment.
- Monitor liver tests at baseline, every month for 6 months during treatment, then periodically as clinically indicated. If increases in ALT, AST or bilirubin related to treatment are suspected, modify OJJAARA dosage based upon Table 1 within the Prescribing Information.

Major Adverse Cardiovascular Events (MACE)

- Another JAK inhibitor increased the risk of MACE, including cardiovascular death, myocardial infarction, and stroke [compared with those treated with tumor necrosis factor (TNF) blockers] in patients with rheumatoid arthritis, a condition for which OJJAARA is not indicated.
- Consider the benefits and risks for the individual patient prior to initiating or continuing therapy with OJJAARA, particularly in patients who are current or past smokers and patients with other cardiovascular risk factors. Inform patients receiving OJJAARA of the symptoms of serious cardiovascular events and the steps to take if they occur.

Thrombosis

- Another JAK inhibitor increased the risk of thrombosis, including deep venous thrombosis, pulmonary embolism, and arterial thrombosis (compared with those treated with TNF blockers) in patients with rheumatoid arthritis, a condition for which OJJAARA is not indicated. Evaluate patients with symptoms of thrombosis and treat appropriately.

Malignancies

- Another JAK inhibitor increased the risk of lymphoma and other malignancies excluding nonmelanoma skin cancer (NMSC) (compared with those treated with TNF blockers) in patients with rheumatoid arthritis, a condition for which OJJAARA is not indicated. Current or past smokers were at increased risk.
- Consider the benefits and risks for the individual patient prior to initiating or continuing therapy with OJJAARA, particularly in patients with a known malignancy (other than a successfully treated NMSC), patients who develop a malignancy, and patients who are current or past smokers.

Adverse Reactions

- The most common adverse reactions (≥20% in either study) are thrombocytopenia, hemorrhage, bacterial infection, fatigue, dizziness, diarrhea, and nausea.

Organic Anion Transporting Polypeptide (OATP)1B1/B3 Inhibitors

- Momelotinib is an OATP1B1/B3 substrate. Concomitant use with an OATP1B1/B3 inhibitor increases momelotinib maximal concentrations (C_{max}) and area under the concentration-time curve (AUC), which may increase the risk of adverse reactions with OJJAARA. Monitor patients concomitantly receiving an OATP1B1/B3 inhibitor for adverse reactions and consider OJJAARA dose modifications.

Breast Cancer Resistance Protein (BCRP) Substrates

- Momelotinib is a BCRP inhibitor. OJJAARA may increase exposure of BCRP substrates, which may increase the risk of BCRP substrate adverse reactions. When administered concomitantly with OJJAARA, initiate rosuvastatin (BCRP substrate) at 5 mg and do not increase to more than 10 mg once daily. Dose adjustment of other BCRP substrates may also be needed. Follow approved product information recommendations for other BCRP substrates.

Pregnancy

- Available data in pregnant women are insufficient. OJJAARA should only be used during pregnancy if the expected benefits to the mother outweigh the potential risks to the fetus.

Lactation

- It is not known whether OJJAARA is excreted in human milk. Because of the potential for serious adverse reactions in a breastfed child, patients should not breastfeed during treatment with OJJAARA, and for at least 1 week after the last dose of OJJAARA.

Females and Males of Reproductive Potential

- Advise females of reproductive potential who are not pregnant to use highly effective contraception during therapy and for at least 1 week after the last dose of OJJAARA.

Hepatic Impairment

- Momelotinib exposure increased with severe hepatic impairment (Child-Pugh C). The recommended starting dose of OJJAARA in patients with severe hepatic impairment (Child-Pugh C) is 150 mg orally once daily. No dose modification is recommended for patients with mild hepatic impairment (Child-Pugh A) or moderate hepatic impairment (Child-Pugh B).

Please see full Prescribing Information, including Patient Information, for OJJAARA.

GSK in oncology

GSK is committed to maximizing patient survival through transformational medicines, with a current focus on breakthroughs in immuno-oncology and tumor-cell targeting therapies, and development in hematologic malignancies, gynecologic cancers and other solid tumors.

About GSK

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.

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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 under Item 3.D 'Risk factors" in the company's Annual Report on Form 20-F for 2022, and Q2 Results for 2023 and any impacts of the COVID-19 pandemic.

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