Stock-exchange announcement

For media and investors only

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Jemperli (dostarlimab-gxly) plus chemotherapy approved in the US as the first new frontline treatment option in decades for dMMR/MSI-H primary advanced or recurrent endometrial cancer

- *Jemperli* is the only immuno-oncology treatment approved in the frontline setting for this patient population in combination with chemotherapy
- Patients with this type of endometrial cancer face significant unmet need and typically experience poor long-term outcomes with the current standard of care

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GSK plc (LSE/NYSE: GSK) today announced that the US Food and Drug Administration (FDA) has approved *Jemperli* (dostarlimab-gxly) in combination with carboplatin and paclitaxel, followed by *Jemperli* as a single agent for the treatment of adult patients with primary advanced or recurrent endometrial cancer that is mismatch repair deficient (dMMR), as determined by an FDA-approved test, or microsatellite instability-high (MSI-H). The supplemental Biologics License Application (sBLA) supporting this new indication received Priority Review and was approved ahead of the Prescription Drug User Fee Act action date.

Hesham Abdullah, Senior Vice President, Global Head of Oncology Development, GSK, said: "Today's expanded approval of *Jemperli* redefines the treatment landscape for patients with dMMR/MSI-H primary advanced or recurrent endometrial cancer. Until now, chemotherapy alone has been the standard of care with many patients experiencing disease progression. In the RUBY trial, *Jemperli* plus chemotherapy demonstrated a 71% reduction in the risk of disease progression or death versus chemotherapy in this patient population, providing a statistically significant and clinically meaningful benefit. These results and today's approval underscore our belief in the potential for *Jemperli* to transform cancer treatment as a backbone immuno-oncology therapy."

With this approval, *Jemperli* is now indicated earlier in treatment in combination with chemotherapy for patients with dMMR/MSI-H primary advanced or recurrent endometrial cancer. *Jemperli* is already approved in the US as monotherapy in adult patients with dMMR recurrent or advanced endometrial cancer that has progressed on or following a prior platinum-containing regimen in any setting and are not candidates for curative surgery or radiation.

Matthew Powell, MD, Chief, Division of Gynecologic Oncology, Washington University School of Medicine, and US principal investigator of the RUBY trial said: "As a clinician, I celebrate the practice-changing potential of adding *Jemperli* to chemotherapy for patients with dMMR/MSI-H primary advanced or recurrent endometrial cancer who have had limited treatment options. Based on the results from the RUBY clinical trial, I look forward to the addition of *Jemperli* to chemotherapy becoming a new standard of care for patients."

Wenora Johnson, President, Board of Directors, Facing Our Risk of Cancer Empowered (FORCE) said: "The endometrial cancer community is thrilled by today's news, which changes the treatment paradigm for a population with long-term unmet needs. FORCE is grateful for the many participants and researchers who contributed to this important study. As an endometrial cancer survivor, I know how much this approval offers hope for patients with primary advanced or recurrent dMMR/MSI-H endometrial cancer."

The FDA approval is supported by interim analysis results from Part 1 of the RUBY/ENGOT-EN6/GOG3031/NSGO phase III trial, which reflect a robust median duration of follow-up of ≥ 25 months. The trial met the primary endpoint of investigator-assessed progression-free survival (PFS), demonstrating a statistically significant and clinically meaningful benefit in patients treated with *Jemperli* plus carboplatin and paclitaxel in the dMMR/MSI-H population. In the dMMR/MSI-H population, a 71% reduction in the risk of disease progression or death was observed. Part 1 of the RUBY trial continues to assess overall survival (OS) in the intent-to-treat (ITT) population, a dual-primary endpoint alongside investigator-assessed PFS.

The safety and tolerability profile for *Jemperli* plus carboplatin and paclitaxel was generally consistent with the known safety profiles of the individual agents. The most common treatment-emergent adverse events (≥ 20%) in patients receiving *Jemperli* plus chemotherapy were rash, diarrhea, hypothyroidism and hypertension.

The RUBY trial data were presented at the European Society for Medical Oncology (ESMO) Virtual Plenary and Society of Gynecologic Oncology (SGO) Annual Meeting on 27 March 2023, and were simultaneously published in *The New England Journal of Medicine*.

The sBLA supporting this new indication was reviewed under the FDA Oncology Center of Excellence Project Orbis Framework, which allowed for concurrent submission to and review by US and other international regulatory authorities. As part of Project Orbis, the application remains under review in Australia, Canada, Switzerland, Singapore and the United Kingdom. A marketing authorization application is also under review by the European Medicines Agency.

About endometrial cancer
Endometrial cancer is one of the most common gynecologic cancers in developed countries,[1] and there are about 60,000 new cases of endometrial cancer diagnosed every year in the US. [2] Approximately 15-20% of patients with endometrial cancer will be diagnosed with advanced disease at the time of diagnosis. [3] [4] An estimated 20-29% of all endometrial cancers are dMMR/MSI-H.[5] Chemotherapy used alone has been the current standard of care for primary advanced or recurrent endometrial cancer, and many patients eventually experience disease progression.[6]

About RUBY
RUBY is a two-part global, randomized, double-blind, multicenter phase III trial of patients with primary advanced or recurrent endometrial cancer. Part 1 is evaluating dostarlimab-gxly plus carboplatin-paclitaxel followed by dostarlimab-gxly versus carboplatin-paclitaxel plus placebo followed by placebo. Part 2 is evaluating dostarlimab-gxly plus carboplatin-paclitaxel followed by dostarlimab-gxly plus niraparib versus placebo plus carboplatin-paclitaxel followed by placebo.

The dual-primary endpoints in Part 1 are investigator-assessed PFS based on the Response Evaluation Criteria in Solid Tumors v1.1 and OS. The statistical analysis plan included pre-specified analyses of PFS in the dMMR/MSI-H and ITT populations and OS in the overall population. Pre-specified exploratory analyses of PFS in the mismatch repair proficient (MMRp)/microsatellite stable (MSS) population and OS in the dMMR/MSI-H populations were also performed. RUBY Part 1 included a broad population, including histologies often excluded from clinical trials and had approximately 10% of patients with carcinosarcoma and 20% with serous carcinoma. In Part 2, the primary endpoint is investigator-assessed PFS. Secondary endpoints in Part 1 and Part 2 include PFS per blinded independent central review, overall response rate, duration of response, disease control rate, patient-reported outcomes, and safety and tolerability.

About *Jemperli* (dostarlimab-gxly)
Jemperli is a programmed death receptor-1 (PD-1)-blocking antibody that binds to the PD-1 receptor and blocks its interaction with the PD-1 ligands PD-L1 and PD-L2. [7]

Jemperli was discovered by AnaptysBio, Inc. and licensed to TESARO, Inc., under a collaboration and exclusive license agreement signed in March 2014. The collaboration has resulted in three monospecific antibody therapies that have progressed into the clinic. These are: *Jemperli* (GSK4057190), a PD-1 antagonist; cobolimab,

(GSK4069889), a TIM-3 antagonist; and GSK4074386, a LAG-3 antagonist. GSK is responsible for the ongoing research, development, commercialisation, and manufacturing of each of these medicines under the agreement.

Indications and Important Safety Information for JEMPERLI (dostarlimab-gxly)

- JEMPERLI, in combination with carboplatin and paclitaxel, followed by JEMPERLI as a single agent, is indicated for the treatment of adult patients with primary advanced or recurrent endometrial cancer (EC) that is mismatch repair deficient (dMMR), as determined by an FDA-approved test, or microsatellite instability-high (MSI-H).
- JEMPERLI, as a single agent, is indicated for the treatment of adult patients with dMMR recurrent or advanced:
    - EC, as determined by an FDA-approved test, that has progressed on or following prior treatment with a platinum-containing regimen in any setting and are not candidates for curative surgery or radiation, or
    - solid tumors, as determined by an FDA-approved test, that have progressed on or following prior treatment and who have no satisfactory alternative treatment options. This indication is approved under accelerated approval based on tumor response rate and durability of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

Important Safety Information

Severe and Fatal Immune-Mediated Adverse Reactions

- Immune-mediated adverse reactions, which can be severe or fatal, can occur in any organ system or tissue and can occur at any time during or after treatment with a PD-1/PD-L1–blocking antibody, including JEMPERLI.
- Monitor closely for signs and symptoms of immune-mediated adverse reactions. Evaluate liver enzymes, creatinine, and thyroid function tests at baseline and periodically during treatment. For suspected immune-mediated adverse reactions, initiate appropriate workup to exclude alternative etiologies, including infection. Institute medical management promptly, including specialty consultation as appropriate.
- Based on the severity of the adverse reaction, withhold or permanently discontinue JEMPERLI. In general, if JEMPERLI requires interruption or discontinuation, administer systemic corticosteroids (1 to 2 mg/kg/day prednisone or equivalent) until improvement to ≤Grade 1. Upon improvement to ≤Grade 1, initiate corticosteroid taper and continue to taper over at least 1 month. Consider administration of other systemic immunosuppressants in patients whose immune-mediated adverse reaction is not controlled with corticosteroids.

Immune-Mediated Pneumonitis

- JEMPERLI can cause immune-mediated pneumonitis, which can be fatal. In patients treated with other PD-1/PD-L1–blocking antibodies, the incidence of pneumonitis is higher in patients who have received prior thoracic radiation. Pneumonitis occurred in 2.3% (14/605) of patients, including Grade 2 (1.3%), Grade 3 (0.8%), and Grade 4 (0.2%) pneumonitis.

Immune-Mediated Colitis

- Colitis occurred in 1.3% (8/605) of patients, including Grade 2 (0.7%) and Grade 3 (0.7%) adverse reactions. Cytomegalovirus infection/reactivation have occurred in patients with corticosteroid-refractory immune-mediated colitis. In such cases, consider repeating infectious workup to exclude alternative etiologies.

Immune-Mediated Hepatitis

- JEMPERLI can cause immune-mediated hepatitis, which can be fatal. Grade 3 hepatitis occurred in 0.5% (3/605) of patients.

Immune-Mediated Endocrinopathies

- Adrenal Insufficiency
  - Adrenal insufficiency occurred in 1.2% (7/605) of patients, including Grade 2 (0.5%) and Grade 3 (0.7%). For Grade 2 or higher adrenal insufficiency, initiate symptomatic treatment per institutional guidelines, including hormone replacement as clinically indicated. Withhold or permanently discontinue JEMPERLI depending on severity.
- Hypophysitis
  - JEMPERLI can cause immune-mediated hypophysitis. Grade 3 hypophysitis occurred in 0.4% (1/241) of patients receiving JEMPERLI in combination with carboplatin and paclitaxel. Grade 2 hypophysitis occurred in 0.2% (1/605) of patients receiving JEMPERLI as a single agent. Initiate hormone replacement as clinically indicated. Withhold or permanently discontinue JEMPERLI depending on severity.
- Thyroid Disorders
  - Grade 2 thyroiditis occurred in 0.5% (3/605) of patients. Grade 2 hypothyroidism occurred in 12% (28/241) of patients receiving JEMPERLI in combination with carboplatin and paclitaxel. Grade 2 hypothyroidism occurred in 8% (46/605) of patients receiving JEMPERLI as a single agent. Hyperthyroidism occurred in 3.3% (8/241) of patients receiving JEMPERLI in combination with carboplatin and paclitaxel, including Grade 2 (2.9%) and Grade 3 (0.4%). Hyperthyroidism occurred in 2.3% (14/605) of patients receiving JEMPERLI as a single agent, including Grade 2 (2.1%) and Grade 3 (0.2%). Initiate thyroid hormone replacement or medical management of hyperthyroidism as clinically indicated. Withhold or permanently discontinue JEMPERLI depending on severity.
- Type 1 Diabetes Mellitus, Which Can Present with Diabetic Ketoacidosis
  - JEMPERLI can cause type 1 diabetes mellitus, which can present with diabetic ketoacidosis. Grade 3 type 1 diabetes mellitus occurred in 0.4% (1/241) of patients receiving JEMPERLI in combination with carboplatin and paclitaxel. Grade 3 type 1 diabetes mellitus occurred in 0.2% (1/605) of patients receiving JEMPERLI as a single agent. Monitor patients for hyperglycemia or other signs and symptoms of diabetes. Initiate treatment with insulin as clinically indicated. Withhold or permanently discontinue JEMPERLI depending on severity.

Immune-Mediated Nephritis with Renal Dysfunction

- JEMPERLI can cause immune-mediated nephritis, which can be fatal. Grade 2 nephritis, including tubulointerstitial nephritis, occurred in 0.5% (3/605) of patients.

Immune-Mediated Dermatologic Adverse Reactions

- JEMPERLI can cause immune-mediated rash or dermatitis. Bullous and exfoliative dermatitis, including Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), and drug rash with eosinophilia and systemic symptoms (DRESS), have occurred with PD-1/PD-L1–blocking antibodies. Topical emollients and/or topical corticosteroids may be adequate to treat mild to moderate non-bullous/exfoliative rashes. Withhold or permanently discontinue JEMPERLI depending on severity.

Other Immune-Mediated Adverse Reactions

- The following clinically significant immune-mediated adverse reactions occurred in <1% of the 605 patients treated with JEMPERLI or were reported with the use of other PD-1/PD-L1–blocking antibodies. Severe or fatal cases have been reported for some of these adverse reactions.
  - *Nervous System:* Meningitis, encephalitis, myelitis and demyelination, myasthenic syndrome/myasthenia gravis, Guillain-Barré syndrome, nerve paresis, autoimmune neuropathy
  - *Cardiac/Vascular:* Myocarditis, pericarditis, vasculitis
  - *Ocular:* Uveitis, iritis, other ocular inflammatory toxicities. Some cases can be associated with retinal detachment. Various grades of visual impairment to include blindness can occur

- *Gastrointestinal:* Pancreatitis, including increases in serum amylase and lipase levels, gastritis, duodenitis
- *Musculoskeletal and Connective Tissue:* Myositis/polymyositis, rhabdomyolysis and associated sequelae including renal failure, arthritis, polymyalgia rheumatica
- *Endocrine:* Hypoparathyroidism
- *Other (Hematologic/Immune):* Autoimmune hemolytic anemia, aplastic anemia, hemophagocytic lymphohistiocytosis, systemic inflammatory response syndrome, histiocytic necrotizing lymphadenitis (Kikuchi lymphadenitis), sarcoidosis, immune thrombocytopenia, solid organ transplant rejection

Infusion-Related Reactions

- Severe or life-threatening infusion-related reactions have been reported with PD-1/PD-L1–blocking antibodies. Severe infusion-related reactions (Grade 3) occurred in 0.2% (1/605) of patients receiving JEMPERLI. Monitor patients for signs and symptoms of infusion-related reactions. Interrupt or slow the rate of infusion or permanently discontinue JEMPERLI based on severity of reaction.

Complications of Allogeneic HSCT

- Fatal and other serious complications can occur in patients who receive allogeneic hematopoietic stem cell transplantation (HSCT) before or after treatment with a PD-1/PD-L1–blocking antibody, which may occur despite intervening therapy. Monitor patients closely for transplant-related complications and intervene promptly.

Embryo-Fetal Toxicity and Lactation

- Based on its mechanism of action, JEMPERLI can cause fetal harm. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with JEMPERLI and for 4 months after their last dose. Because of the potential for serious adverse reactions from JEMPERLI in a breastfed child, advise women not to breastfeed during treatment with JEMPERLI and for 4 months after their last dose.

Common Adverse Reactions

The most common adverse reactions (≥20%) in patients with dMMR/MSI-H EC who received JEMPERLI in combination with carboplatin and paclitaxel were rash, diarrhea, hypothyroidism, and hypertension. The most common Grade 3 or 4 laboratory abnormalities (≥10%) were decreased neutrophils, decreased hemoglobin, decreased white blood cell count, decreased lymphocytes, increased glucose, decreased sodium, and decreased platelets.

The most common adverse reactions (≥20%) in patients with dMMR EC who received JEMPERLI as a single agent were fatigue/asthenia, anemia, nausea, diarrhea, constipation, vomiting, and rash. The most common Grade 3 or 4 laboratory abnormalities (>2%) were decreased lymphocytes, decreased sodium, increased alanine aminotransferase, increased creatinine, decreased neutrophils, decreased albumin, and increased alkaline phosphatase.
The most common adverse reactions (≥20%) in patients with dMMR solid tumors who received JEMPERLI as a single agent were fatigue/asthenia, anemia, diarrhea, and nausea. The most common Grade 3 or 4 laboratory abnormalities (≥2%) were decreased lymphocytes, decreased sodium, increased alkaline phosphatase, and decreased albumin.

Please see accompanying US Prescribing Information.

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.

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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 us.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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