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US FDA accepts for priority review GSK's application for an expanded indication of *Jemperli* (dostarlimab-gxly) plus chemotherapy to include all adult patients with primary advanced or recurrent endometrial cancer

- Application supported by statistically significant and clinically meaningful progression-free and overall survival data from phase III RUBY Part 1 trial
- Dostarlimab-gxly plus chemotherapy is the only immuno-oncology-based therapy to show a statistically significant and clinically meaningful survival benefit in the overall patient population
- 23 August 2024 assigned as Prescription Drug User Fee Act action date for FDA decision

GSK plc (LSE/NYSE: GSK) today announced the US Food and Drug Administration (FDA) accepted the supplemental Biologics License Application (sBLA) for *Jemperli* (dostarlimab-gxly) in combination with standard-of-care chemotherapy (carboplatin and paclitaxel) to expand treatment to all adult patients with primary advanced or recurrent endometrial cancer. This would include patients with mismatch repair proficient (MMRp)/microsatellite stable (MSS) tumors.

Currently, *Jemperli* is FDA-approved 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 either mismatch repair deficient (dMMR), as determined by an FDA-approved test, or microsatellite instability-high (MSI-H).

The FDA granted Priority Review for this application and assigned a Prescription Drug User Fee Act action date of August 23, 2024.

The sBLA is based on results from Part 1 of the RUBY phase III trial. The trial met its primary endpoints of investigator-assessed progression-free survival (PFS) and overall survival (OS), demonstrating a statistically significant and clinically meaningful benefit in the overall population of patients treated with dostarlimab-gxly plus carboplatin-paclitaxel versus chemotherapy alone. RUBY Part 1 is the only clinical trial to show a statistically significant survival benefit in the overall patient population. The safety and tolerability analysis from RUBY showed a safety profile for dostarlimab-gxly and carboplatin-paclitaxel that was generally consistent with the known safety profiles of the individual agents.

OS data were presented at the Society of Gynecologic Oncology (SGO) Annual Meeting on Women's Cancer on March 16, 2024.

About endometrial cancer

Endometrial cancer is found in the inner lining of the uterus, known as the endometrium. Endometrial cancer is the most common gynecologic cancer in developed countries, with approximately 417,000 new cases reported each year worldwide¹, and incidence rates are expected to rise by almost 40% between 2020 and 2040.^{2,3} Approximately 15-20% of patients with endometrial cancer will be diagnosed with advanced disease at the time of



diagnosis.⁴ Among patients with primary advanced or recurrent endometrial cancer, approximately 70-75% have MMRp/MSS tumors.⁵

About RUBY

RUBY is a two-part global, randomised, 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.

In Part 1, the dual-primary endpoints 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 overall populations and OS in the overall population. Pre-specified exploratory analyses of PFS and OS in the MMRp/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 in the overall population, followed by PFS in the MMRp/MSS population, and OS in the overall population is a key secondary endpoint. Additional secondary endpoints in Part 1 and Part 2 include PFS per blinded independent central review, PFS2, overall response rate, duration of response, disease control rate, patient-reported outcomes, and safety and tolerability.

RUBY is part of an international collaboration between the European Network of Gynaecological Oncological Trial groups (ENGOT), a research network of the European Society of Gynaecological Oncology (ESGO) that consists of 22 trial groups from 31 European countries that perform cooperative clinical trials, and the GOG Foundation, a non-profit organization dedicated to transforming the standard of care in gynecologic oncology.

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-L2.⁶

Jemperli was discovered by AnaptysBio, Inc. and licensed to TESARO, Inc., under a collaboration and exclusive license agreement signed in March 2014. Under this agreement, GSK is responsible for the ongoing research, development, commercialization, and manufacturing of *Jemperli*, and cobolimab (GSK4069889), a TIM-3 antagonist.

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 \leq Grade 1. Upon improvement to \leq 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 palsy, 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, other transplant (including corneal graft) 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 ($\geq 20\%$) 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 ($\geq 10\%$) were decreased neutrophils, decreased hemoglobin, decreased white blood cell count, decreased lymphocytes, increased glucose, decreased sodium, and decreased platelets.

The most common adverse reactions ($\geq 20\%$) 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 ($\geq 20\%$) 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 ($\geq 2\%$) were decreased lymphocytes, decreased sodium, increased alkaline phosphatase, and decreased albumin.

Please see the full [US Prescribing Information](#) for JEMPERLI.

GSK in oncology

Oncology is an emerging therapeutic area for GSK where we are committed to maximizing patient survival with a current focus on hematologic malignancies, gynecologic cancers and other solid tumors through breakthroughs in immuno-oncology and tumor-cell targeting therapies.

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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Press release

For media and investors only



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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 2023.

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References

1. Faizan U, Muppidi V. Uterine Cancer. [Updated 2022 Sep 5]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan. Available at: www.ncbi.nlm.nih.gov/books/NBK562313/.
2. Braun MM, et al. Am Fam Physician. 2016;93(6):468-474.
3. International Research on Cancer. Global Cancer Observatory. Cancer Tomorrow. Gco.iarc.fr/tomorrow/en/dataviz/. Accessed 23 Apr 2024.
4. CMP: CancerMPact® Patient Metrics Mar-2023, Cerner Enviza. Available at www.cancermpact.com. Accessed 23 Apr 2024.
5. Based on CMP:CancerMPact® [Patient Metrics], Cerner Enviza. Available from www.cancermpact.com. Accessed 23 Apr 2024.
6. Laken H, Kehry M, Mcneeley P, et al. Identification and characterization of TSR-042, a novel anti-human PD-1 therapeutic antibody. European Journal of Cancer. 2016;69, S102. doi:10.1016/s0959-8049(16)32902-1.