Press release

For media and investors only

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Jemperli (dostarlimab-gxly) trial continues to show unprecedented results with no evidence of disease in 100% of patients with locally advanced mismatch repair deficient (dMMR) rectal cancer

- Updated analysis from Memorial Sloan Kettering Cancer Center presented at ASCO 2024 has expanded to 42 patients with clinical complete response
- New treatment options are needed for patients facing negative impacts to quality-of-life with current standard of care
- Additional registrational studies of dostarlimab-gxly in dMMR/microsatellite instability-high rectal (MSI-H) and colorectal cancer are recruiting

GSK plc (LSE/NYSE: GSK) today announced updated, longer-term results from the phase II supported collaborative study with Memorial Sloan Kettering Cancer Center (MSK) evaluating *Jemperli* (dostarlimab-gxly) as a first-line treatment—as an alternative to surgery—for mismatch repair deficient (dMMR) locally advanced rectal cancer. The trial showed an unprecedented 100% clinical complete response rate (cCR) in 42 patients who completed treatment with dostarlimab-gxly, defined as complete pathologic response or no evidence of tumors as assessed by magnetic resonance imaging, endoscopy and digital rectal exam. In the first 24 patients evaluated, a sustained clinical complete response with a median follow-up of 26.3 months (95% CI: 12.4-50.5) was observed.

These late-breaking data are being presented today at the 2024 American Society of Clinical Oncology (ASCO) Annual Meeting (May 31 – June 4) in Chicago, IL as a rapid oral presentation (abstract LBA3512). The latest research presented today from the phase II trial builds on the findings initially presented in a late-breaking presentation at the 2022 ASCO Annual Meeting with simultaneous publication in *The New England Journal of Medicine*.[1]

Hesham Abdullah, Senior Vice President, Global Head Oncology, R&D, GSK, said: "The data showing no evidence of disease in 42 patients is remarkable. These results bring us one step closer to understanding the potential of dostarlimab-gxly in this curative-intent setting for patients with dMMR locally advanced rectal cancer. We look forward to evaluating dostarlimab-gxly in certain colorectal cancers in our ongoing AZUR-1 and AZUR-2 registrational studies."

The current standard of care (SoC) for patients with dMMR/microsatellite instability-high (MSI-H) locally advanced rectal cancer is initial treatment with chemotherapy plus radiation followed by surgery to remove the tumor along with portions of the intestine and/or surrounding tissue.[1] This results in initial positive outcomes for most patients, but nearly one-third ultimately die from cancer that has spread to other parts of the body (distant metastasis).[2] Additionally, the surgery and chemoradiotherapy associated with SoC can lead to long-term adverse effects that have a significantly negative impact on quality of life, including bowel, urinary and sexual dysfunction, secondary cancers and infertility.[1]

Andrea Cercek, MD, Section Head of Colorectal Cancer and Co-Director of the Center for Young Onset Colorectal and Gastrointestinal Cancer, MSK, and Principal Investigator of the phase II study said: "These findings demonstrate the potential of dostarlimab-gxly as a novel approach to treating locally advanced dMMR rectal

cancer that leads to durable complete tumor regression without the need for life-altering treatment. As a clinician, I've seen firsthand the debilitating impact of standard treatment of dMMR rectal cancer and am thrilled about the potential of dostarlimab-gxly in these patients."

The safety and tolerability profile of dostarlimab-gxly was generally consistent with the known safety profile of the agent. No adverse events of grade 3 or higher were reported in this trial.

Dostarlimab-gxly is not approved anywhere in the world for the frontline treatment of locally advanced dMMR rectal cancer. GSK is advancing studies evaluating dostarlimab-gxly in patients with advanced/metastatic stages of dMMR/MSI-H colorectal cancer through its AZUR clinical trial programme. AZUR-1 is a global, multi-center, open-label, phase II registrational clinical trial investigating the efficacy and safety of dostarlimab-gxly as monotherapy – as a replacement for chemotherapy, radiation and/or surgery – for treatment-naïve patients with dMMR/MSI-H locally advanced rectal cancer. The AZUR-1 trial aims to confirm the findings of the supported collaborative study in locally advanced dMMR rectal cancer led by Dr. Cercek at MSK. AZUR-2 is a phase III trial evaluating the efficacy of perioperative dostarlimab-gxly compared with SoC in participants with untreated T4N0 or Stage III (resectable) dMMR/MSI-H colon cancer.

About dMMR/MSI-H rectal cancer
Rectal cancer is a form of cancer that starts in the rectum, the final section of the large intestine, and is often categorized as part of a group of cancers called colorectal cancer.[3] Colorectal cancer is the third most commonly diagnosed cancer in the world.[4] In the US, it is estimated that approximately 46,220 individuals are diagnosed annually with rectal cancer.[5] Approximately 5-10% of all rectal cancers are mismatch repair deficient (dMMR)/microsatellite instability-high (MSI-H), meaning that they contain abnormalities that affect the proper repair of DNA when copied in a cell.[6] Mismatch repair deficient status is a biomarker that has been shown to predict response to immune checkpoint blockade with PD-1 therapy.[7,8] Tumors with this biomarker are most commonly found in endometrial, colorectal and other gastrointestinal cancers but may also be found in other solid tumors.[9-11]

About *Jemperli*
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.[12]

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 ≤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, 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 (≥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 the full US Prescribing Information for JEMPERLI.

GSK in oncology

Oncology is an emerging therapeutic area for GSK where we are committed to maximzing 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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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 GSK's Annual Report on Form 20-F for 2023, and GSK's Q1 Results for 2024.

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Dr. Cercek has financial interests related to GSK.

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