Press release

For media and investors only

Issued: 3 June 2024, London UK

Jemperli (dostarlimab) 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 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) 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, defined as complete pathologic response or no evidence of tumours 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 (31 May – 4 June) 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 in this curative-intent setting for patients with dMMR locally advanced rectal cancer. We look forward to evaluating dostarlimab 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 tumour 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 as a novel approach to treating locally advanced dMMR rectal

cancer that leads to durable complete tumour 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 in these patients."

The safety and tolerability profile of dostarlimab 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 is not approved anywhere in the world for the frontline treatment of locally advanced dMMR rectal cancer. GSK is advancing studies evaluating dostarlimab in patients with advanced/metastatic stages of dMMR/MSI-H colorectal cancer through its AZUR clinical trial programme. AZUR-1 is a global, multi-centre, open-label, phase II registrational clinical trial investigating the efficacy and safety of dostarlimab 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 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 categorised 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] Tumours with this biomarker are most commonly found in endometrial, colorectal and other gastrointestinal cancers but may also be found in other solid tumours.[9-12]

About *Jemperli* (dostarlimab)
Jemperli, a programmed death receptor-1 (PD-1)-blocking antibody, is the backbone of GSK's ongoing immuno-oncology-based research and development programme. A robust clinical trial programme includes studies of *Jemperli* alone and in combination with other therapies in gynaecologic, colorectal and lung cancers, as well as where there are opportunities for transformational outcomes. It is the first and only immuno-oncology treatment approved, in combination with chemotherapy, in the frontline setting for primary advanced or recurrent dMMR/MSI-H endometrial cancer.

In the US, *Jemperli* is indicated 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 dMMR, as determined by a US FDA-approved test, or MSI-H, and as a single agent for adult patients with dMMR recurrent or advanced endometrial cancer, as determined by a US FDA-approved test, that has progressed on or following a prior platinum-containing regimen in any setting and are not candidates for curative surgery or radiation. The sBLA supporting this indication in combination with carboplatin and paclitaxel for dMMR/MSI-H primary advanced or recurrent endometrial cancer received Breakthrough Therapy designation and Priority Review from the US FDA. *Jemperli* is also indicated in the US for patients with dMMR recurrent or advanced solid tumours, as determined by a US FDA-approved test, that have progressed on or following prior treatment and who have no satisfactory alternative treatment options. The latter indication is approved in the US under accelerated approval based on tumour response rate and durability of response. Continued approval for this indication in solid tumours may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

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, commercialisation, and manufacturing of *Jemperli*, and cobolimab (GSK4069889), a TIM-3 antagonist.

Important Information for *Jemperli* in the EU

Indication

***Jemperli* is indicated:**

- in combination with carboplatin-paclitaxel, for the treatment of adult patients with mismatch repair deficient (dMMR)/microsatellite instability-high (MSI-H) primary advanced or recurrent endometrial cancer and who are candidates for systemic therapy;
- as monotherapy for treating adult patients with mismatch repair deficient (dMMR)/microsatellite instability-high (MSI-H) recurrent or advanced endometrial cancer that has progressed on or following prior treatment with a platinum-containing regimen.

Refer to the *Jemperli* EMA Reference Information for a full list of adverse events and the complete important safety information in the EU here: https://www.ema.europa.eu/en/medicines/human/EPAR/jemperli.

GSK in oncology

Oncology is an emerging therapeutic area for GSK where we are committed to maximising patient survival with a current focus on haematologic malignancies, gynaecologic cancers, and other solid tumours through breakthroughs in immuno-oncology and tumour-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 gsk.com.

GSK enquiries

Media:	Tim Foley	+44 (0) 20 8047 5502	(London)
	Dan Smith	+44 (0) 20 8047 5502	(London)
	Kathleen Quinn	+1 202 603 5003	(Washington DC)
	Lyndsay Meyer	+1 202 302 4595	(Washington DC)
Investor Relations:	Nick Stone	+44 (0) 7717 618834	(London)
	James Dodwell	+44 (0) 20 8047 2406	(London)
	Mick Readey	+44 (0) 7990 339653	(London)
	Josh Williams	+44 (0) 7385 415719	(London)
	Camilla Campbell	+44 (0) 7803 050238	(London)
	Steph Mountifield	+44 (0) 7796 707505	(London)
	Jeff McLaughlin	+1 215 751 7002	(Philadelphia)
	Frannie DeFranco	+1 215 751 4855	(Philadelphia)

Registered in England & Wales:
No. 3888792

Registered Office:
980 Great West Road
Brentford, Middlesex

TW8 9GS

Dr. Cercek has financial interests related to GSK.

References

[1] Cercek A, Lumish M, Sinopoli J, et al. PD-1 blockade in mismatch repair–deficient, locally advanced rectal cancer. N Engl J Med 2022; 386: 2363-76.
[2] Smith JJ, et al. Rectal Cancer Consortium. Organ Preservation in Rectal Adenocarcinoma: a phase II randomized controlled trial evaluating 3-year disease-free survival in patients with locally advanced rectal cancer treated with chemoradiation plus induction or consolidation chemotherapy, and total mesorectal excision or nonoperative management. BMC Cancer. 2015 Oct 23;15:767. doi: 10.1186/s12885-015-1632-z. PMID: 26497495; PMCID: PMC4619249.
[3] Sung H, Ferlay J, Siegel RL, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J Clin. 2021;71(3):209-249. doi:10.3322/caac.21660.
[4] SEER Explorer. SEER Explorer Application. Accessed April 19, 2024. Available at https://seer.cancer.gov/statistics-network/explorer/.
[5] Siegel RL, Giaquinto AN, Jemal A. Cancer statistics, 2024. *CA Cancer J Clin*. 2024;74(1):12-49. Doi:10.3322/caac.21820.
[6] Cercek A, et al. Mismatch Repair-Deficient Rectal Cancer and Resistance to Neoadjuvant Chemotherapy. Clin Cancer Res. 2020 Jul 1;26(13):3271-3279. doi: 1158/1078-0432.CCR-19-3728. Epub 2020 Mar 6. PMID: 32144135; PMCID: PMC7348681.
[7] Le DT, et al. PD-1 blockade in tumors with mismatch repair deficiency. N Engl J Med. 2015;372(26):2509-2520.
[8] Marabelle A, et al. Efficacy of pembrolizumab in patients with noncolorectal high microsatellite instability/mismatch repair deficient cancer: results from the Phase II KEYNOTE-158 study. J Clin Oncol. 2020;38(1):1-10.
[9] National Cancer Institute at the National Institutes of Health. Definition of mismatch repair deficiency. Accessed April 19, 2024. Available at: https://www.cancer.gov/publications/dictionaries/cancer-terms/def/mismatch-repair-deficiency.
[10] Lorenzi M, et al. Epidemiology of microsatellite instability high (MSI-H) and deficient mismatch repair (dMMR) in solid tumors: a structured literature review. J Oncol. 2020. doi.org/10.1155/2020/1807929.
[11] Zhao P, et al. Mismatch repair deficiency/microsatellite instability-high as a predictor for anti-PD-1/PD-L1 immunotherapy efficacy. J Hematol Oncol. 2019;12(1):54. doi: 10.1186/s13045-019-0738-1.
[12] 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.