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Jemperli (dostarlimab) receives US FDA Breakthrough Therapy Designation for locally advanced dMMR/MSI-H rectal cancer

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- **Designation based on data showing no evidence of disease in 100% of all 42 patients who completed treatment with dostarlimab**
- **Breakthrough Therapy Designation granted to drugs with potential to show improvement over available therapies for serious conditions**
- **Current standard of care can be associated with significant negative quality-of-life effects, highlighting the need for new options**

GSK plc (LSE/NYSE: GSK) announced today that the US Food and Drug Administration (FDA) has granted Breakthrough Therapy Designation for *Jemperli*

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dostarlimab) for the treatment of patients with locally advanced mismatch repair deficient (dMMR)/microsatellite instability-high (MSI-H) rectal cancer. The Breakthrough Therapy Designation aims to expedite the development and review of drugs with the potential to treat a serious condition and where preliminary clinical evidence may indicate substantial improvement over currently available therapy.[1] This is the second regulatory designation for dostarlimab in locally advanced dMMR/MSI-H rectal cancer, following Fast Track designation for the same patient population in January 2023.[2]

Hesham Abdullah, Senior Vice President, Global Head Oncology, R&D, GSK, said: "Today's designation, which is based on the unprecedented 100% clinical complete response rate of dostarlimab reported to date, supports a path to help change the treatment paradigm for patients with locally advanced dMMR/MSI-H rectal cancer, who face long-term adverse quality-of-life effects. Our registrational AZUR-1 trial is continuing to study dostarlimab in this patient population."

The US FDA's Breakthrough Therapy Designation is supported by preliminary clinical evidence from the ongoing phase II GSK supported collaborative study with Memorial Sloan Kettering Cancer Center. In frontline locally advanced dMMR rectal cancer, the trial has shown an unprecedented 100% clinical complete response (cCR) in all 42 patients who completed treatment with dostarlimab, defined as no evidence of tumours as assessed by magnetic resonance imaging, endoscopy, PET scan and digital rectal exam. In the first 24 patients evaluated, a sustained cCR with a median follow-up of 26.3 months (95% CI: 12.4-50.5) was observed. 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.[3] The trial continues to evaluate enrolled patients. GSK's ongoing phase II registrational AZUR-1 trial in locally advanced dMMR/MSI-H rectal cancer aims to confirm the findings of this supported collaborative study.

The current standard of care for patients with dMMR/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.[4] 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).[5] Additionally, the surgery and chemoradiotherapy associated with standard of care can lead to long-term negative impact on quality-of-life, including bowel, urinary and sexual dysfunction, secondary cancers and infertility.[2]

Dostarlimab is not approved anywhere in the world for the frontline treatment of locally advanced dMMR/MSI-H rectal cancer.

‹bout 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. Colorectal cancer is the third most commonly diagnosed cancer in the world.[6] In the US, it is estimated that approximately 46,220 individuals are diagnosed annually with rectal cancer.[7] Approximately 5-10% of all rectal cancers are dMMR/MSI-H, meaning that they contain abnormalities that affect the proper repair of DNA when copied in a cell.[8] Mismatch repair deficient status is a biomarker that has been shown to predict response to immune checkpoint blockade with PD-1 therapy.[9,10] Tumours with this biomarker are most commonly found in endometrial, colorectal and other gastrointestinal cancers but may also be found in other solid tumours.[11-14]

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.

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. This includes patients with mismatch repair proficient/microsatellite stable (MMRp/MSS) and dMMR/MSI-H tumours. *Jemperli* is also approved 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. Additionally, *Jemperli* is 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

Jemperli is indicated:

- in combination with carboplatin and 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.

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.

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 Q3 Results for 2024.

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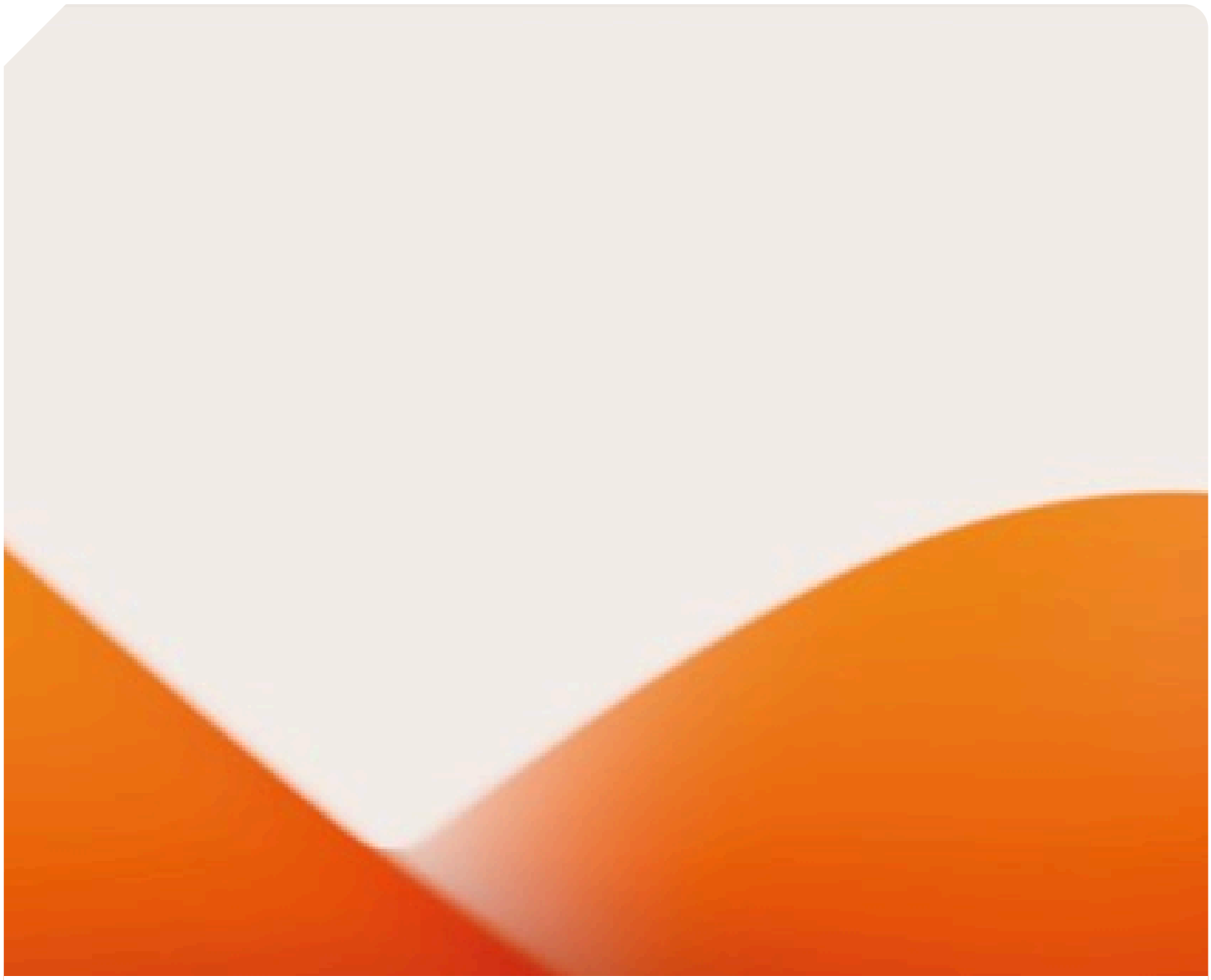

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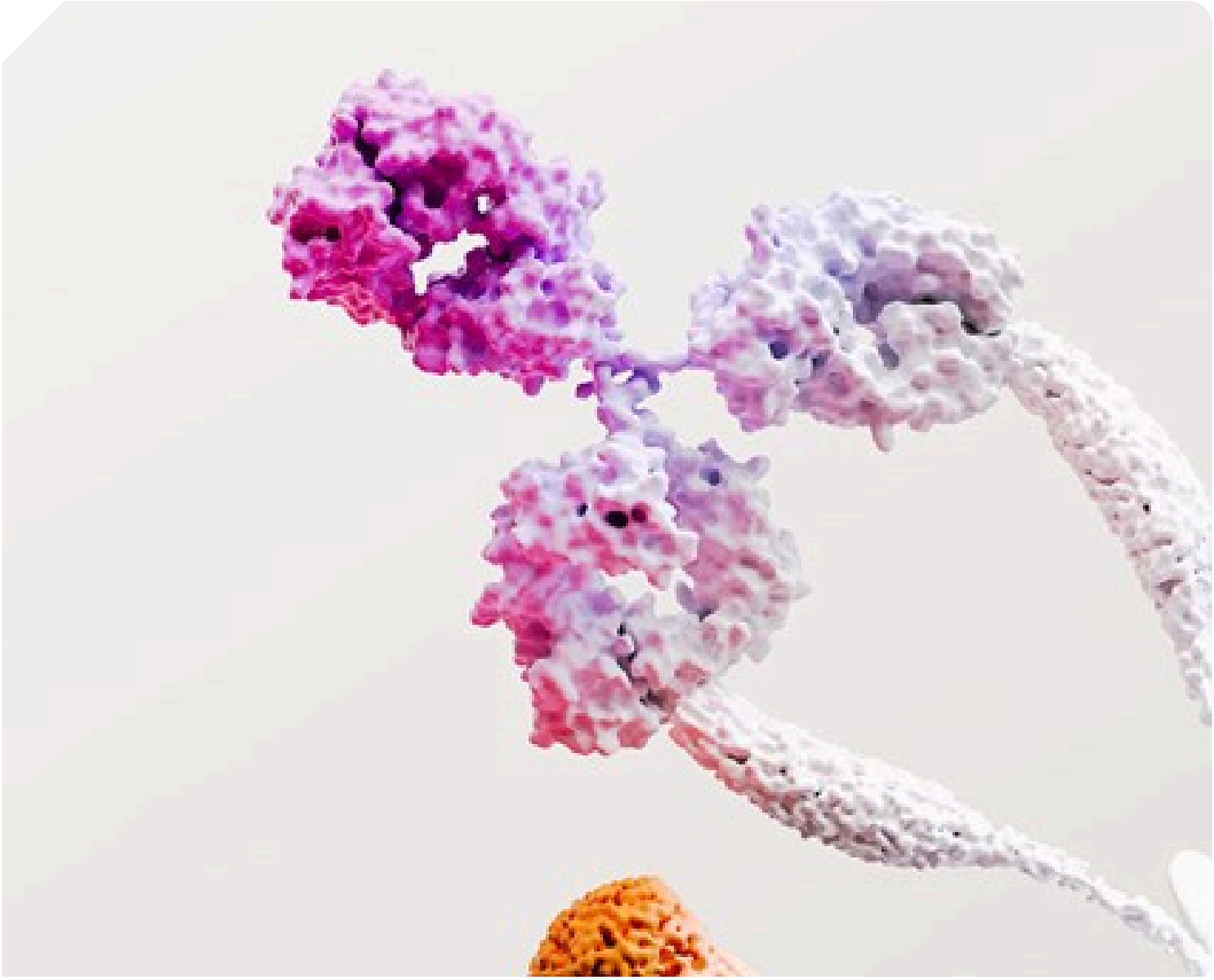

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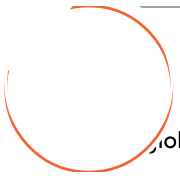

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