US FDA Advisory Committee votes in support of trials designed to evaluate Jemperli (dostarlimab-gxly) as a potential treatment for mismatch repair-deficient/microsatellite instability-high locally advanced rectal cancer

PUBLISHED FEB 9, 2023
BY GSK

For media and investors only

- US FDA also recently granted Fast Track designation to Jemperli in this patient population

GSK plc (LSE/NYSE: GSK) today announced that the US Food and Drug Administration (FDA) Oncologic Drugs Advisory Committee (ODAC) voted 8 to 5 in support of the question posed to the committee regarding whether data from two proposed single-arm trials will be

> sufficient to characterize the benefits and risks

of Jemperli (dostarlimab-gxly) in the curative-intent setting for patients with mismatch repair-deficient/microsatellite instability-high (dMMR/MSI-H) locally advanced rectal cancer.

Hesham Abdullah, Senior Vice President, Global Head of Oncology Development, GSK, said:

> The Committee's positive vote in favour of our proposed clinical trial programme for dostarlimab reinforces our plans to generate data in support of a future US regulatory submission

for the potential treatment of patients with dMMR/MSI-H locally advanced rectal cancer, a patient population with significant unmet medical needs and a standard of care that results in serious quality of life concerns. We thank the committee for the constructive dialogue and we look forward to continued interactions with FDA as we progress our development programme.

The current standard of care (SoC) for patients with dMMR/MSI-H locally advanced rectal cancer is neoadjuvant chemoradiotherapy (CRT) followed by surgery and adjuvant chemotherapy. Neoadjuvant CRT provides local tumour control in most patients, but nearly one-third ultimately die from distant metastasis. Additionally, SoC is associated with long-term adverse effects, including bowel, urinary and sexual dysfunction, secondary malignancy and infertility i.

As part of its proposed clinical trial programme, GSK is initiating a global, open-label, phase II clinical trial to investigate 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 primary endpoint of GSK's proposed trial is clinical complete response for 12 months (cCR12) as assessed by Independent Central Review. Key secondary endpoints will include cCR for 36 months and event-free survival for three years by investigator assessment. In addition, the trial aims to confirm results generated in a separate ongoing investigator-initiated trial by researchers at Memorial Sloan Kettering Cancer Center (MSK). Researchers at MSK shared these findings in a late-breaking presentation at the 2022 American Society of Clinical Oncology (ASCO) Annual Meeting with simultaneous publication in The New England Journal of Medicine.i GSK intends to use data from the Company's proposed trial, alongside data from MSK's ongoing trial of 30 patients, to support a supplemental Biologics License Application (sBLA) for accelerated regulatory approval in this indication.

In January 2023, the US FDA granted dostarlimab-gxly Fast Track designation for the treatment of dMMR/MSI-H locally advanced rectal cancer. Fast Track designation is designed to accelerate the development and expedite the review of potential new medicines to treat serious conditions with unmet medical needs. In addition, the application could be eligible for priority review if supported by clinical

data at the time of the submission to the FDA.

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. Colorectal cancer is the third most commonly diagnosed cancer in the world. In the US, it is estimated that approximately 20,220 individuals are diagnosed annually with rectal cancer. 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. Mismatch repair-deficient status is a biomarker that has been shown to predict response to immune checkpoint blockade with PD-1 therapy. Tumours with this biomarker are most commonly found in endometrial, colorectal and other gastrointestinal cancers but may also be found in other solid tumours.

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. GSK's ambition is for dostarlimab to become the backbone of the Company's ongoing immuno-oncology-based research and development programme when used alone and in combination with standard of care and future novel cancer therapies, particularly in patients with currently limited treatment options. Dostarlimab is being investigated in registrational enabling trials as monotherapy and as part of combination regimens, including in women with recurrent or primary advanced endometrial cancer, women with Stage III or IV non-mucinous epithelial ovarian cancer, and patients with other advanced solid tumours or metastatic cancers. Dostarlimab has not been approved anywhere in the world as monotherapy for treatment-naïve patients with dMMR/MSI-H locally advanced rectal cancer. The US FDA has granted dostarlimab Fast Track designation for the treatment of dMMR/MSI-H locally advanced rectal cancer.

Dostarlimab 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: dostarlimab (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.

Important Information for Jemperli in the EU

Jemperli is indicated as monotherapy for the treatment of 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 Reference Information for a full list of adverse events and the complete important safety information in the EU.

GSK is committed to maximising patient survival through transformational medicines. GSK's oncology pipeline is focused on immuno-oncology, tumour cell targeting therapies and synthetic lethality. Our goal is to achieve a sustainable flow of new treatments based on a diversified portfolio of investigational medicines utilising modalities such as small molecules, antibodies, and antibody-drug conjugates, either alone or in combination.

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/company.

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 in the Company's Annual Report on Form 20-F for 2021, GSK's Q4 Results for 2022 and any impacts of the COVID-19 pandemic.

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.

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.

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

SEER Explorer. SEER Explorer Application. Accessed February 9, 2023, from https://seer.cancer.gov/statistics-network/explorer/.

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: 10.1158/1078-0432.CCR-19-3728. Epub 2020 Mar 6. PMID: 32144135; PMCID: PMC7348681.

Le DT, et al. PD-1 blockade in tumors with mismatch repair deficiency. N Engl J Med. 2015;372(26):2509-2520.

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.

National Cancer Institute at the National Institutes of Health. Definition of mismatch repair deficiency. Available at: https://www.cancer.gov/publications/dictionaries/cancer-terms/.... Accessed May 5, 2021.

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.

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.

Press release distributed by Wire Association on behalf of GSK, on Feb 9, 2023. For more information subscribe and follow us.

Media Assets

Embedded Media

Visit the online press release to interact with the embedded media.

https://wireassociation.eu/newsroom/gsk/releases/en/us-fda-advisory-committee-votes-in-support-of-trials-designed-to-evaluate-jemperli-dostarlimab-gxly-as-a-potential-treatment-for-mismatch-repair-deficientmicrosatellite-instability-high-locally-advanced-rectal-cancer-1781

GSK

Newsroom: https://wireassociation.eu/newsroom/gsk
Website: https://www.gsk.com/
Primary Email: corporate.media@gsk.com

Social Media

Facebook - https://www.facebook.com/GSK
Twitter - http://twitter.com/GSK
Youtube - http://www.youtube.com/GSK
Linkedin - http://www.linkedin.com/company/glaxosmithkline
Instagram - https://www.instagram.com/gsk/