Press release

For media and investors only

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Positive RUBY phase III data show potential for *Jemperli* (dostarlimab) combinations in more patients with primary advanced or recurrent endometrial cancer

- Dostarlimab plus chemotherapy is the only immuno-oncology combination to show statistically significant and clinically meaningful overall survival (OS) in the overall population

- 31% reduction in risk of death and 16.4-month improvement in median OS observed with dostarlimab plus chemotherapy versus chemotherapy in the overall population

- 37% reduction in risk of disease progression or death and 6-month improvement in median progression-free survival observed with the addition of *Zejula* (niraparib) to dostarlimab maintenance following dostarlimab plus chemotherapy versus chemotherapy in MMRp/MSS population where treatment options are still needed

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GSK plc (LSE/NYSE: GSK) today announced statistically significant and clinically meaningful overall survival (OS) results from Part 1 and progression-free survival (PFS) results from Part 2 of the RUBY/ENGOT-EN6/GOG3031/NSGO phase III trial in adult patients with primary advanced or recurrent endometrial cancer. These data were presented today in a late-breaking plenary session at the Society of Gynecologic Oncology 2024 Annual Meeting on Women's Cancer (16-18 March).

The goal of the RUBY phase III trial programme is to evaluate which patients with primary advanced or recurrent endometrial cancer could potentially benefit from treatment with *Jemperli* (dostarlimab) plus chemotherapy, with or without the addition of *Zejula* (niraparib) maintenance. Part 1 of the RUBY phase III trial is investigating dostarlimab plus standard-of-care chemotherapy (carboplatin-paclitaxel) followed by dostarlimab compared to chemotherapy plus placebo followed by placebo. Part 2 of the RUBY phase III trial is evaluating dostarlimab plus standard-of-care chemotherapy, followed by dostarlimab plus niraparib as maintenance therapy compared to chemotherapy plus placebo followed by placebo. The safety and tolerability profiles of dostarlimab plus carboplatin-paclitaxel and dostarlimab plus carboplatin-paclitaxel followed by dostarlimab plus niraparib were generally consistent with the known safety profiles of the individual medicines.

Previous data showed a statistically significant and clinically meaningful improvement in PFS with *Jemperli* plus chemotherapy versus chemotherapy alone in frontline mismatch repair deficient (dMMR)/microsatellite instability-high (MSI-H) primary advanced or recurrent endometrial cancer. These data led to regulatory approvals for this patient population in the US, EU and certain other countries. Data presented today show additional potential benefit of dostarlimab plus chemotherapy, with or without the addition of niraparib, in the overall population of patients with primary advanced or recurrent endometrial cancer, including patients with mismatch repair proficient (MMRp)/microsatellite stable (MSS) tumours, for which there are currently no approved immuno-therapy-based regimens.

Hesham Abdullah, Senior Vice President, Global Head Oncology, R&D, GSK said: "The positive data presented today further show how dostarlimab-based regimens could benefit a broader set of patients with endometrial cancer. The results we've seen to date comprise the growing body of evidence supporting the role of dostarlimab as the backbone of our immuno-oncology development programme. Our goal is to continue to identify ways to use dostarlimab alone and in combination with other therapies to help improve outcomes for patients with limited treatment options."

RUBY Part 1: a statistically significant and clinically meaningful improvement in OS was observed for dostarlimab plus chemotherapy versus placebo plus chemotherapy, meeting a primary endpoint of the study.
Dostarlimab plus chemotherapy versus chemotherapy alone showed:

In the overall population:
- a statistically significant reduction in the risk of death by 31% (Hazard Ratio [HR]: 0.69; [95% CI: 0.539–0.890])
- a clinically meaningful improvement of 16.4 months in median OS (44.6 months vs 28.2 months)

In a prespecified exploratory analysis of the MMRp/MSS population:
- a clinically meaningful trend in reduced risk of death by 21% (HR: 0.79; [95% CI: 0.602–1.044])
- a clinically meaningful improvement of seven months in median OS (34.0 months vs 27.0 months)

Full OS summaries are shown below.

	dostarlimab + carboplatin-paclitaxel	placebo + carboplatin-paclitaxel
Overall population, Number (N)	245	249
OS, HR (95% CI)	0.69 (0.539–0.890)	
P-value[1]	0.002	
OS, median (95% CI), mo.	44.6 (32.6–NR)	28.2 (22.1–35.6)
dMMR/MSI-H population[2], N	53	65
OS, HR (95% CI)	0.32 (0.166–0.629)	
OS, median[3] (95% CI), mo.	NR (NR–NR)	31.4 (20.3–NR)
MMRp/MSS[2], N	192	184
OS, HR (95% CI)	0.79 (0.602–1.044)	
OS, median (95% CI), mo.	34.0 (28.6–NR)	27.0 (21.5–35.6)

[1] One-sided p-value based on stratified log-rank test.
[2] Exploratory analyses of OS in dMMR/MSI-H and OS in MMRp/MSS populations were pre-specified with no planned hypothesis testing.
[3] Although the median OS was not reached, at 30 months the estimated reduction in the risk of death was 82.8% for patients who received dostarlimab plus chemotherapy vs. 54.1% for patients who received chemotherapy alone.

Matthew Powell, MD, Division of Gynecologic Oncology, Washington University School of Medicine, and US principal investigator of the RUBY trial said: "RUBY Part 1 is the first clinical trial to show a statistically significant and clinically meaningful improvement in overall survival for an immuno-oncology therapy in combination with chemotherapy in the overall population of patients with primary advanced or recurrent endometrial cancer. As a

clinician, I celebrate the results of the RUBY Part 1 trial presented today, which show how dostarlimab added to chemotherapy could potentially benefit a broader set of patients with this type of cancer."

In RUBY Part 1, grade 3 or higher and serious treatment-emergent adverse events (AEs) were approximately 12% higher in the dostarlimab plus carboplatin-paclitaxel arm (treatment arm) compared with the placebo plus carboplatin-paclitaxel arm (control arm). The nature and types of immune-related AEs in the dostarlimab plus chemotherapy safety profile were consistent with the mechanism of action of dostarlimab and similar to those reported for other PD-(L)1 inhibitors. In the trial, 40.7% of participants in the treatment arm and 16.3% of participants in the control arm had immune-related AEs assessed by the investigator as related to dostarlimab or placebo, respectively. Discontinuation of dostarlimab or placebo due to a treatment-emergent AE occurred in 19.1% of patients in the treatment arm and 8.1% of patients in the control arm.

GSK expects US Food and Drug Administration regulatory submission acceptance based on RUBY Part 1 data for an expanded indication in the overall population in the first half of this year.

RUBY Part 2: addition of niraparib to dostarlimab in maintenance setting significantly improved PFS in first-line primary advanced or recurrent endometrial cancer compared to chemotherapy alone, meeting the primary endpoint of the trial.

Dostarlimab plus chemotherapy followed by dostarlimab plus niraparib compared to placebo plus chemotherapy followed by placebo showed:

In the overall population:

- a statistically significant reduction in the risk of disease progression or death by 40% (HR: 0.60 [95% CI: 0.43–0.82])
- a clinically meaningful improvement of 6.2 months in median PFS (14.5 months vs 8.3 months)

In the MMRp/MSS population:

- a statistically significant reduction in the risk of disease progression or death by 37% (HR: 0.63 [95% CI: 0.44–0.91])
- a clinically meaningful improvement of 6.0 months in median PFS (14.3 months vs 8.3 months)

Dr Mansoor Raza Mirza, Chief Oncologist, Copenhagen University Hospital, Denmark, and RUBY principal investigator said: "In RUBY Part 2, we observed that the use of dostarlimab in combination with niraparib in the maintenance therapy setting further improved progression-free survival versus placebo for patients with primary advanced or recurrent endometrial cancer. These findings are particularly important for patients who have MMRp/MSS tumours as the data help build on the initial benefit observed with an immuno-oncology plus chemotherapy regimen, reflecting the potential for the addition of niraparib maintenance to address unmet medical need for these patients."

In RUBY Part 2, grade 3 or higher and serious treatment-emergent AEs were approximately 36% and 24% higher, respectively, in the dostarlimab plus chemotherapy followed by dostarlimab plus niraparib arm (treatment arm) compared with the placebo plus chemotherapy followed by placebo arm (control arm). In the trial, 36.6% of participants in the treatment arm and 6.3% of participants in the control arm had immune-related AEs assessed by the investigator as related to dostarlimab or placebo, respectively. No cases of myelodysplastic syndrome/acute myeloid leukaemia were reported; other secondary primary malignancies occurred in 1 patient each in both treatment arms. Discontinuation of dostarlimab or placebo due to a TEAE occurred in 24.1% of patients in the treatment arm and 5.2% of patients in the control arm. Discontinuation of niraparib or placebo due to a treatment-emergent AE occurred in 15.7% of patients in the treatment arm and 4.2% of patients in the control arm.

About endometrial cancer

Endometrial cancer is found in the inner lining of the uterus, known as the endometrium. Endometrial cancer is the most common gynaecologic cancer in developed countries, with approximately 417,000 new cases reported each year worldwide[1], 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]

About RUBY
RUBY is a two-part global, randomised, double-blind, multicentre phase III trial of patients with primary advanced or recurrent endometrial cancer. Part 1 is evaluating dostarlimab plus carboplatin-paclitaxel followed by dostarlimab versus carboplatin-paclitaxel plus placebo followed by placebo. Part 2 is evaluating dostarlimab plus carboplatin-paclitaxel followed by dostarlimab 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 Tumours 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 organisation dedicated to transforming the standard of care in gynaecologic oncology.

About *Jemperli* (dostarlimab)
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.[5]

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 supplemental Biologics License Application supporting the newly approved 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.

About *Zejula* (niraparib)
Zejula is an oral, once-daily poly(ADP-ribose) polymerase (PARP) inhibitor indicated in the US for the maintenance treatment of adult patients with advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in complete or partial response to first-line platinum-based chemotherapy; and for the maintenance treatment of adult patients with deleterious or suspected deleterious germline *BRCA*-mutated recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to platinum-based chemotherapy and who have been selected based on a US FDA-approved companion diagnostic for *Zejula*.

Important Information for *Zejula* in the EU

Indication
Zejula is indicated:
- as monotherapy for the maintenance treatment of adult patients with advanced epithelial (FIGO Stages III and IV) high-grade ovarian, fallopian tube or primary peritoneal cancer who are in response (complete or partial) following completion of first-line platinum-based chemotherapy.
- as monotherapy for the maintenance treatment of adult patients with platinum-sensitive relapsed high-grade serous epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in response (complete or partial) to platinum-based chemotherapy.

Refer to the *Zejula* 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.

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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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