New data presented at ASH 2021 highlight potential of Blenrep (belantamab mafodotin-blmf) in combination with standard of care therapies in earlier lines of multiple myeloma treatment

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For media and investors only

- DREAMM-9 phase I initial results demonstrate overall response rates (ORR) of 100% in three dosing cohorts and 83% in two dosing cohorts in newly diagnosed patients

- Data suggest potential of optimising dosing for belantamab mafodotin and will help inform further studies

GlaxoSmithKline (GSK) plc today announced new data from the DREAMM-9 (DRiving Excellence in Approaches to Multiple Myeloma) phase I trial and two GSK collaborative studies investigating the potential use of Blenrep (belantamab mafodotin-blmf), a first-in-class anti-BCMA (B-cell maturation antigen) therapy, in combination with standard of care therapies in earlier lines of multiple myeloma treatment. These data were presented at the 63rd American Society of Hematology (ASH) Annual Meeting and Exposition.

Collectively, the data from these trials suggest that with an optimised dose, schedule and combination treatment, corneal events associated with belantamab mafodotin may be reduced in patients receiving earlier lines of therapy. These data will be used to help inform further studies evaluating the potential of belantamab mafodotin in a broader patient population.

DREAMM-9 trial (abstract #2738) – Preliminary results from this phase I trial evaluating a quadruplet combination treatment regimen of

belantamab mafodotin with standard of care (bortezomib, lenalidomide and dexamethasone [VRd]) in transplant-ineligible patients with newly diagnosed multiple myeloma (n=36) demonstrated lower rates of corneal events in the cohorts with extended dose schedules and lower doses, while maintaining a high ORR.

Dosing across the five cohorts in DREAMM-9 trial varies. Cohort 1 is 1.9 mg/kg Q3/4W; Cohort 2 is 1.4 mg/kg Q6/8W; Cohort 3 is 1.9 mg/kg Q6/8W; Cohort 4 is 1.0 mg/kg Q3/4W and Cohort 5 is 1.4 mg/kg Q3/4W. An ORR of 100% was observed in Cohorts 1 (n=12), 3 and 5 (n=6) and an ORR of 83% was observed in Cohorts 2 and 4 (n=5/6). At least 50% of patients in each cohort achieved a very good partial response (VGPR) or better, with the highest rates observed in Cohorts 1 and 5 (100% in each). In Cohort 1, 7 out of 9 patients achieved minimal residual disease (MRD)-negative status at the first test after a VGPR.

Hesham Abdullah, Global Head of Oncology Development, GSK, said:

> We remain committed to addressing unmet needs by evaluating belantamab mafodotin in earlier lines of treatment in combination with standard of care therapies, as well as assessing different dosing regimens to optimise efficacy and safety in these settings. These promising data at ASH, while early-stage, underscore the importance of exploring the potential of belantamab mafodotin as part of combination regimens to improve outcomes for patients with multiple myeloma.

There were no new adverse events (AEs) associated with belantamab mafodotin in DREAMM-9. The majority of patients experienced treatment-related AEs, which were generally managed with dose modifications. The most common AEs leading to dose modifications were thrombocytopenia, neutropenia and corneal AEs. All patients experiencing corneal AEs remained on treatment.

Dr Saad Z. Usmani, Chief of Myeloma Service, Memorial Sloan Kettering Cancer Center and DREAMM-9 principal investigator said:

> For patients with newly diagnosed multiple myeloma who are not eligible for a stem cell transplant, the exploration of novel frontline combination therapies are critical to improving survival. We believe these initial results from the DREAMM-9

clinical trial demonstrate the potential of combination therapy with belantamab mafodotin, with a majority of patients achieving a very good partial response or better and consistent safety findings, underscoring how this may become an important treatment regimen for these patients.

BelaRd trial (abstract #2736) – Preliminary results from the BelaRd trial evaluating the triplet combination of belantamab mafodotin with lenalidomide and dexamethasone (Rd) demonstrated an ORR of 100% (n=18) across the three cohorts (2.5 mg/kg Q8W, 1.9 mg/kg Q8W, 1.4 mg/kg Q8W), furthering evidence of the potential of belantamab mafodotin in transplant-ineligible patients with newly diagnosed multiple myeloma. A trial being led by the Hellenic Society of Hematology in collaboration with GSK in treatment-naïve patients, BelaRd found no new safety signals. Across all three dosing cohorts, no grade 3 or greater corneal AEs were observed.

ALGONQUIN (abstract #1653) – Updated results from ALGONQUIN, a trial led by the Canadian Myeloma Research Group in collaboration with GSK, evaluating belantamab mafodotin in combination with pomalidomide/dexamethasone (PomDex) in patients with relapsed/refractory multiple myeloma (2.5 median prior lines of therapy) were also presented. Across all dosing cohorts (n=54), belantamab mafodotin plus PomDex resulted in an ORR of 88.9%, with 72.2% achieving a VGPR or better and a median progression-free survival (mPFS) of 17 months (95% CI, 14.5-not yet reached). Belantamab mafodotin administered as 2.5 mg/kg Q8W (n=12) demonstrated an ORR of 83.3%, with a mPFS that has not yet been reached (95% CI, 11.3-not yet reached). This dosing schedule has been selected for the Part 2 cohort expansion based on optimised safety and efficacy. The current FDA-recommended dose of single-agent belantamab mafodotin is 2.5 mg/kg administered Q3W.

The combination therapy of belantamab mafodotin and PomDex in the ALGONQUIN trial demonstrated a safety profile that is consistent with the known safety profiles of belantamab mafodotin and PomDex individually. Among patients evaluable for safety (n=56), treatment-related AEs were reported by 96.4% of patients; the most frequent non-ocular grade 3 or greater events included neutropenia and thrombocytopenia. Serious AEs were observed in 50% of patients, with one fatal event due to acute respiratory distress syndrome. Two patients (3.6%) discontinued due to AEs, including one case of

leukoencephalopathy (2.5 mg/kg Q4W; unlikely related to treatment) and elevated ALT (2.5 mg/kg Q12W, possibly related to treatment).

Blenrep is an anti-BCMA treatment that received accelerated and conditional approvals in the US and the EU, respectively, for adult patients with relapsed/refractory multiple myeloma who have received at least four prior therapies, including an anti-CD38 antibody, a proteasome inhibitor and an immunomodulatory agent. Blenrep is not currently approved in any other treatment setting, including in newly diagnosed multiple myeloma or for use in combination with other multiple myeloma therapies.

DREAMM-9 is a randomised, multi-cohort, dose and schedule evaluation trial to investigate the safety, pharmacokinetics, pharmacodynamics and clinical activity of belantamab mafodotin administered in combination with standard of care (bortezomib, lenalidomide and dexamethasone [VRd]) in patients with transplant-ineligible newly diagnosed multiple myeloma. Initial results were presented at ASH and included five cohorts evaluating different doses of belantamab mafodotin in combination with VRd: 1.9 mg/kg Q3/4W (Cohort 1), 1.4 mg/kg Q6/8W (Cohort 2), 1.9 mg/kg Q6/8W (Cohort 3), 1.0 mg/kg Q3/4W (Cohort 4) and 1.4 mg/kg Q3/4W (Cohort 5). All patients received VRd Q3W until cycle 8, followed by lenalidomide plus dexamethasone Q4W.

BelaRd is phase I/II, open-label trial designed to assess the safety and clinical activity of different belantamab mafodotin doses in combination with lenalidomide and dexamethasone (Rd) in treatment-naïve, transplant-ineligible, newly diagnosed multiple myeloma. The trial, which is being conducted in Greece, is comprised of two distinct parts: Part 1 will evaluate different doses of belantamab mafodotin in combination with Rd in up to three cohorts and will determine the recommended Part 2 dose to be further evaluated for safety and clinical activity in the dose expansion cohort (Part 2). The recommended Part 2 dose will be used for future trials in the transplant-ineligible, newly diagnosed multiple myeloma setting. Part 2 of the trial will also evaluate an alternative dose modification schedule to assess the impact on corneal adverse events.

ALGONQUIN is a phase I/II trial being conducted in Canada and is investigating belantamab mafodotin in combination with PomDex in patients with relapsed/refractory multiple myeloma who had received

≥2 prior lines of treatment, were exposed to lenalidomide and a proteasome inhibitor and were refractory to their last line of therapy. This trial consists of a Part 1 dose-finding portion and a Part 2 expansion phase. Initial data from the Part 1 phase of the trial was presented at ASH 2020 and identified 2.5 mg/kg in combination with standard dosing of PomDex as the maximum tolerated dose. At ASH 2021, updated safety and efficacy data and additional dosing cohorts used to identify the recommended Part 2 dose were presented. The following dosing of belantamab mafodotin was evaluated: 1.92 mg/kg or 2.5 mg/kg Q4W, 2.5 mg/kg loading dose followed by 1.92 mg/kg Q4W from cycle 2 onwards, 2.5 mg/kg Q8W or Q12W and 2.5 mg/kg or 3.4 mg/kg split equally on day 1 and 8 Q4W. Pom was administered at 4 mg on days 1-21 and Dex was administered at 40 mg (20 mg for age > 75 years) weekly.

Multiple myeloma is the second most common blood cancer in the US and is generally considered treatable, but not curable., In the US, more than 32,000 people are estimated to be diagnosed with multiple myeloma this year and nearly 13,000 people will die from the disease. Research into new therapies is needed as multiple myeloma commonly becomes refractory to available treatments.

About B-cell maturation antigen (BCMA)

The normal function of BCMA is to promote plasma cell survival by transduction of signals from two known ligands, BAFF (B-cell activating factor) and APRIL (a proliferation-inducing ligand). This pathway has been shown to be important for myeloma cell growth and survival. BCMA expression is limited to B cells at later stages of development. BCMA is expressed at varying levels in myeloma patients and BCMA membrane expression is universally detected in myeloma cell lines.

Blenrep is an antibody drug conjugate comprising a humanised BCMA monoclonal antibody conjugated to the cytotoxic agent auristatin F via a non-cleavable linker. The drug linker technology is licensed from Seagen; monoclonal antibody is produced using POTELLIGENT Technology licensed from BioWa Inc. a member of the Kyowa Kirin Group.

BLENREP is indicated for the treatment of adults with relapsed or refractory multiple myeloma who have received at least 4 prior therapies, including an anti-CD38 monoclonal antibody, a proteasome

inhibitor, and an immunomodulatory agent.

This indication is approved under accelerated approval based on response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

IMPORTANT US SAFETY INFORMATION

BLENREP caused changes in the corneal epithelium resulting in changes in vision, including severe vision loss and corneal ulcer, and symptoms such as blurred vision and dry eyes.

Conduct ophthalmic exams at baseline, prior to each dose, and promptly for worsening symptoms. Withhold BLENREP until improvement and resume, or permanently discontinue, based on severity.

Because of the risk of ocular toxicity, BLENREP is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the BLENREP REMS.

Ocular Toxicity: Ocular adverse reactions occurred in 77% of the 218 patients in the pooled safety population. Ocular adverse reactions included keratopathy (76%), changes in visual acuity (55%), blurred vision (27%), and dry eye (19%). Among patients with keratopathy (n = 165), 49% had ocular symptoms, 65% had clinically relevant visual acuity changes (decline of 2 or more lines on Snellen Visual Acuity in any eye), and 34% had both ocular symptoms and visual acuity changes.

Keratopathy: Keratopathy was reported as Grade 1 in 7% of patients, Grade 2 in 22%, Grade 3 in 45%, and Grade 4 in 0.5% per the KVA scale. Cases of corneal ulcer (ulcerative and infective keratitis) have been reported. Most keratopathy events developed within the first 2 treatment cycles (cumulative incidence of 65% by Cycle 2). Of the patients with Grade 2 to 4 keratopathy (n = 149), 39% recovered to Grade 1 or lower after median follow-up of 6.2 months. Of the 61% who had ongoing keratopathy, 28% were still on treatment, 9% were in follow-up, and in 24% the follow-up ended due to death, study withdrawal, or lost to follow-up. For patients in whom events resolved, the median time to resolution was 2 months (range: 11 days to 8.3 months).

Visual Acuity Changes: A clinically significant decrease in visual acuity of worse than 20/40 in the better-seeing eye was observed in 19% of the 218 patients and of 20/200 or worse in the better-seeing eye in 1.4%. Of the patients with decreased visual acuity of worse than 20/40, 88% resolved and the median time to resolution was 22 days (range: 7 days to 4.2 months). Of the patients with decreased visual acuity of 20/200 or worse, all resolved and the median duration was 22 days (range: 15 to 22 days).

Monitoring and Patient Instruction: Conduct ophthalmic examinations (visual acuity and slit lamp) at baseline, prior to each dose, and promptly for worsening symptoms. Perform baseline examinations within 3 weeks prior to the first dose. Perform each follow-up examination at least 1 week after the previous dose and within 2 weeks prior to the next dose. Withhold BLENREP until improvement and resume at same or reduced dose, or consider permanently discontinuing based on severity. Advise patients to use preservative-free lubricant eye drops at least 4 times a day starting with the first infusion and continuing until end of treatment. Avoid use of contact lenses unless directed by an ophthalmologist. Changes in visual acuity may be associated with difficulty for driving and reading. Advise patients to use caution when driving or operating machinery. BLENREP is only available through a restricted program under a REMS.

Thrombocytopenia: Thrombocytopenia occurred in 69% of 218 patients in the pooled safety population, including Grade 2 in 13%, Grade 3 in 10%, and Grade 4 in 17%. The median time to onset of the first thrombocytopenic event was 26.5 days. Thrombocytopenia resulted in dose reduction, dose interruption, or discontinuation in 9%, 2.8%, and 0.5% of patients, respectively. Grade 3 to 4 bleeding events occurred in 6% of patients, including Grade 4 in 1 patient. Fatal adverse reactions included cerebral hemorrhage in 2 patients. Perform complete blood cell counts at baseline and during treatment as clinically indicated. Consider withholding and/or reducing the dose based on severity.

Infusion-Related Reactions: Infusion-related reactions occurred in 18% of 218 patients in the pooled safety population, including Grade 3 in 1.8%. Monitor patients for infusion-related reactions. For Grade 2 or 3 reactions, interrupt the infusion and provide supportive treatment. Once symptoms resolve, resume at a lower infusion rate. Administer

premedication for all subsequent infusions. Discontinue BLENREP for life-threatening infusion-related reactions and provide appropriate emergency care.

Embryo-Fetal Toxicity: Based on its mechanism of action, BLENREP can cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with BLENREP and for 4 months after the last dose. Advise males with female partners of reproductive potential to use effective contraception during treatment with BLENREP and for 6 months after the last dose. Pregnancy testing is recommended for females of reproductive potential prior to initiating BLENREP.

The pooled safety population described in Warnings and Precautions reflects exposure to BLENREP at a dosage of 2.5 mg/kg or 3.4 mg/kg (1.4 times the recommended dose) administered intravenously once every 3 weeks in 218 patients in DREAMM-2. Of these patients, 194 received a liquid formulation (not the approved dosage form) rather than the lyophilized powder.

Patients received BLENREP at the recommended dosage of 2.5 mg/kg administered intravenously once every 3 weeks (n = 95). Permanent discontinuation due to an adverse reaction occurred in 8% of patients who received BLENREP; keratopathy (2.1%) was the most frequent adverse reaction resulting in permanent discontinuation. Dosage interruptions due to an adverse reaction occurred in 54% of patients who received BLENREP. Adverse reactions which required a dosage interruption in >3% of patients included keratopathy (47%), blurred vision (5%), dry eye (3.2%), and pneumonia (3.2%). Dose reductions due to an adverse reaction occurred in 29% of patients. Adverse reactions which required a dose reduction in >3% of patients included keratopathy (23%) and thrombocytopenia (5%).

The most common adverse reactions (≥20%) were keratopathy (71%), decreased visual acuity (53%), nausea (24%), blurred vision (22%), pyrexia (22%), infusion-related reactions (21%), and fatigue (20%). The most common Grade 3 or 4 (≥5%) laboratory abnormalities were lymphocytes decreased (22%), platelets decreased (21%), hemoglobin decreased (18%), neutrophils decreased (9%), creatinine increased (5%), and gamma-glutamyl transferase increased (5%).

Serious adverse reactions occurred in 40% of patients who received

BLENREP. Serious adverse reactions in >3% of patients included pneumonia (7%), pyrexia (6%), renal impairment (4.2%), sepsis (4.2%), hypercalcemia (4.2%), and infusion-related reactions (3.2%). Fatal adverse reactions occurred in 3.2% of patients, including sepsis (1%), cardiac arrest (1%), and lung infection (1%).

USE IN SPECIFIC POPULATIONS

Lactation: Because of the potential for serious adverse reactions in the breastfed child, advise women not to breastfeed during treatment with BLENREP and for 3 months after the last dose.

Females and Males of Reproductive Potential: Based on findings in animal studies, BLENREP may impair fertility in females and males.

Geriatric Use: Of the 218 patients who received BLENREP in DREAMM-2, 43% were aged 65 to less than 75 years and 17% were aged 75 years and older. Keratopathy occurred in 80% of patients aged less than 65 years and 73% of patients aged 65 years and older. Among the 95 patients who received BLENREP at the 2.5-mg/kg dose, keratopathy occurred in 67% of patients aged less than 65 years and 73% of patients aged 65 years and older.

Renal or Hepatic Impairment: The recommended dosage has not been established in patients with severe renal impairment (eGFR 15 to 29 mL/min/1.73 m2) or end-stage renal disease (ESRD) with eGFR 1.5 × ULN and any AST).

Please see full Prescribing Information, including BOXED WARNING and Medication Guide for BLENREP here.

Dr Usmani has provided consulting services to GlaxoSmithKline.

GSK is focused on maximising patient survival through transformational medicines. GSK's pipeline is focused on immuno-oncology, cell therapy, 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, antibody-drug conjugates and cell therapy, either alone or in combination.

GSK is a science-led global healthcare company. For further information please visit www.gsk.com/about-us.

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 2020, GSK's Q3 Results and any impacts of the COVID-19 pandemic.

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