Meet the Management, Oncology
Transcript | 17 June 2024

Nick Stone | Introduction

Slide 1
Hello everyone. Welcome to our next 'Meet GSK Management' event – Getting Ahead of Cancer. This is an interactive event with the presentation sent to our distribution list by email, and you can also find it on gsk.com.

Please turn to slide 2.

Slide 2 | Cautionary statement
This is the usual safe-harbour statement.

Please turn to slide 3 and let me hand over to Luke to share today's focus.

Luke | Introduction

Slide 3 | Today's focus
Thanks Nick. So today, we hope that you gain a better understanding of our material growth opportunities across our key areas of focus in oncology: haematology, gynaecologic cancers and other tumour types.

We'll highlight the future potential of *Blenrep*, which we anticipate to be a multi-blockbuster asset that delivers a favourable benefit-risk profile for multiple myeloma patients in need. We will also discuss our differentiated immuno-oncology combinations, primarily anchored to our anti-PD-1 *Jemperli* as the backbone.

And, given our recent in-licensing of two ADCs from Hansoh, we will detail our future opportunity across solid tumours. And finally, we will walk you through the near-term catalysts that will help us to achieve our stated growth ambitions.

If we can go to Slide 4, please.

Slide 4 | Participants
You will hear from myself, along with Tony Wood, our CSO, and Dr. Evangelos Terpos to walk us through the most recent *Blenrep* data.

And for Q&A, we will also be joined by Nina Mojas, Hesham Abdullah and Mondher Mahjoubi.

Can we just to go to slide 5 now.

Luke | Strategic Overview

Slide 5 | Focused on core therapy areas

As a reminder, GSK focuses on preventing and treating disease in 4 therapy areas. We most recently spoke to you about our progress in Respiratory. And today, we'll cover our emerging Oncology portfolio.

Slide 6, please.

Slide 6 | Oncology is a significant, emerging contributor to our long-term ambitions

Now I don't think I need to tell people on this call that Oncology is an exciting area. We're confident that our oncology strategy, which we will cover shortly, will contribute to our previously committed 2031 GSK ambition, and it has the opportunity to deliver transformative medicines for patients and value for shareholders.

The Growth of our competitive portfolio stems from the potential to achieve clinical outcomes in defined sub-populations. And in the near-term of 2024-2026, we expect our in-line medicines to continue growth. We also anticipate a potential market re-entry of *Blenrep* in 2L multiple myeloma, and this represents upside to our current ambitions.

In the latter part of this decade through to 2031, we expect a shift in sales composition to reflect potential *Blenrep* expansion, the emergence of immuno-oncology combinations and entry of our two ADCs across tumours.

In a moment, Tony will begin our medicine spotlights with *Blenrep* and the recent practice-changing data presented at ASCO.

Please now turn to Slide 7.

Slide 7 | Focused oncology strategy with potential for expansion

GSK Oncology is focused and focused across three core areas: haematology, gynaecologic cancers and other growth opportunities in solid tumours. We've got several modalities – whether they are antibody-drug conjugates, immunotherapy or targeted small molecules –that span these disease areas.

Our haematology portfolio includes *Ojjaara* in myelofibrosis and belantamab mafodotin (or *Blenrep*) in multiple myeloma, offering significant growth opportunity.

Gynaecological cancers will continue to be a cornerstone of our portfolio with *Jemperli* in endometrial cancer and *Zejula* in ovarian. We also have a strong opportunity to strengthen our gynaecological impact with our recently in-licensed B7-H4 ADC from Hansoh.

And lastly, we are gating investment decisions to maximise these medicines in additional solid tumour types where they could deliver transformational efficacy, such as within colorectal cancer, lung and head and neck.

I'll now hand it over to Tony on slide 8.

Tony | *Blenrep*

Slide 8 | Blenrep (belantamab mafodotin)

Thanks, Luke. Please turn to the next slide.

Slide 9 | Multiple myeloma patients cycle through treatment combinations

Multiple myeloma is a complex disease, and new combination treatment options continuing to emerge. With each line of treatment comes accumulating toxicity and decreasing time until the next relapse. What's more, novel modalities often necessitate hospitalisation or inpatient care, particularly for anti-BCMA agents. Importantly, for the 70% of 1L patients who receive lenalidomide, they only benefit from 12-28 months of PFS in 2L and beyond.

With this in mind, future treatment options should address unmet need, namely extending overall survival and time in remission, lowering toxicity, broadening eligibility and treatment accessibility across sites of care.

We are grateful that Dr. Evangelos Terpos, Professor of Haematology at the National and Kapodistrian University of Athens, and a DREAMM-8 Principal Investigator, is able to join us to walk us through recent *Blenrep* data.

Welcome, Dr Terpos, and please turn to slide 10.

Dr Evangelos Terpos | *Blenrep* and data from DREAMM-7, DREAMM-8 and a NDMM study

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Slide 10 | Introduction

I'm Evangelos Terpos, Professor of Heamatology and Director of the Stem Cell Transplantation Unit in the University of Athens in Greece, and I'm going to present to you the data of the novel studies, DREAMM-7, DREAMM-8 and the newly diagnosed transplant ineligible patients with multiple myeloma who received the combination of BelaRd, an investigator-initiated study.

Next slide please.

Slide 11 | DREAMM-7 study design

This is the study design of the DREAMM-7, which included patients with one prior line of therapy and relapsed/refractory multiple myeloma and the treatment schedule included the combination of bortezomib and dexamethasone at the standard schedule. And in the first arm, we had the addition of belantamab mafodotin at a dose of 2.5 milligram per kilogram every three weeks, followed by, after nine cycles, by 2.5 milligram per kilogram every three weeks alone. Or in the Arm B, the addition of daratumumab at the dose of 16 milligram per kilogram weekly for cycles 1 till 3, then every three weeks for cycles 4 to 8, and then after cycle 9, we had a daratumamab monotherapy, so we had a direct comparison between belantamab mafodotin and daratumumab as monotherapy after the eighth cycle so from cycle 9 and afterwards. The primary endpoint was PFS, key secondary endpoints, overall survival, duration of response and MRD.

We had stratification for prior lines of therapy, revised ISS and prior bortezomib use.

Next slide please.

Slide 12 | DREAMM-7: BVd led to a significant increase in PFS vs. DVd

Regarding PFS, you can see that the combination of belantamab, Velcade and dexamethasone (BVd) produced an impressive more than three years median PFS of 36.6 months versus 13.4 months of daratumumab, Velcade (DVd) and dexamethasone with a hazard ratio of 0.41. So BVd demonstrated a statistically significant and clinically meaningful PFS benefit with amedian PFS that was 23 months longer than that of DVd.

Next slide please.

Slide 13 | DREAMM-7: early OS trend favouring BVd vs. DVd

Regarding overall survival, even with this median follow-up of 28 months, you can see that we have a median overall survival that has not been reached in both arms, but the proportion of patients who are alive at 18 months was 84% in BVd and 73% in DVd, offering a hazard ratio of 0.57 that was statistically significant.

So overall survival, so the nearly strong and clinically meaningful trend favoured BVd, and of course, additional overall survival follow-up is ongoing.

Next slide please.

Slide 14 | DREAMM-7: deeper responses with BVd vs. DVd

And this is mainly because of the impressive overall response rate, which was 82.7% in BVd and 71.3% in DVd.

But if we see the quality of the response, it was much more impressive with BVd with at least a complete response in 35% versus 17% of DVd and the MRD negativity rate in complete responders was 25% versus 9.6% in BVd and DVd, respectively, and the VGPR MRD negativity 38.7% versus 17% in the two arms, respectively.

Next slide please.

Slide 15 | DREAMM-7: prespecified subgroup analysis of IRC-assessed PFS

The PFS benefit was consistent favour BVd versus DVd across all the prespecified subgroups, including patients with lenalidomide refractory or high-risk cytogenetic and especially for those patients who are lenalidomide refractory, and this is a big number of patients now and an unmet need you can see.

Next slide please.

Slide 16 | DREAMM-7: subgroup by lenalidomide refractory status

BVd offer a median PFS of 25 months versus 8.6 months of DVd. In the non-lenalidomide refractory patients, the median is more than 3 years and 18 months in BVd and DVd, respectively. But you have also to appreciate that patients who are lenalidomide refractory were more heavily pre-treated with three or more prior lines of therapy in 42% of the patients in BVd compared to 19% in the same arm for those who were not lenalidomide refractory.

Next slide please.

Slide 17 | DREAMM-7: subgroup by cytogenetic risk

Regarding high risk also, we can appreciate that BVd offered the hazard ratio of 0.31 those with high risk cytogenetic, offering a median PFS of 33.2 months versus 10.5 only in DVd. For the standard risk patients, also BVd continues to have a median PFS, which has – which is 36.6 months versus 15.3 months in the DVd with a hazard ratio of 0.44.

Next slide please.

Slide 18 | DREAMM-8: study design

The DREAMM-8 study was a study that included relapsed refractory patients with one prior line of therapy, but all of them have been exposed to lenalidomide. So a more focused study on lenalidomide explored in refractory patients. In that study, bortezomib, pomalidomide and dexamethasone, which is one of the standard of care was compared tobelantamab mafodotin, pomalidomide and dexamethasone.

Pomalidomide and dexamethasone was given at the standard dose like bortezomib in the Arm B, while in belantamab, we had a very nice schedule with a dose of 2.5 milligram per kilogram given at cycle 1 only every four weeks now, and then followed by 1.9 milligram per kilogram every four weeks from cycle 2 and onward. And there was stratification for prior lines of therapy, priorbortezomib and prior anti-CD38 therapy while the primary endpoint was PFS and key secondary endpoints included overall survival, MRD negativity and duration of response.

Next slide please.

Slide 19 | DREAMM-8: BPd led to a significant PFS benefit vs. PVd

The median PFS has not been reached for the belantamab, pomalidomide and dexamethasone arm, while the 12-month probability of progression-free is 71% versus 51% in PVd. In PVd, the median PFS is 12.7 months that is expected also based on the OPTIMISMM study that gave approval to this combination. The hazard ratio is 0.52.

Next slide please.

Slide 20 | DREAMM-8: PFS benefit was seen consistently across all prespecified subgroups

Regarding the different pre-specified subgroups in the PFS, we've seen benefit with belantamab-PomDex in all these prespecified subgroups, including patients with high-risk cytogenetic, as you can see here, with a hazard ratio of 0.57, but especially to patients who are refractory to lenalidomide with the hazard ratio of 0.45.

Next slide please.

Slide 21 | DREAMM-8: PFS benefit was seen consistently across all prespecified subgroups

And patients who are refractory to anti-CD38 monoclonal antibody, either daratumumab or isatuximab with a hazard ratio of 0.65.

Next slide please.

Slide 22 | DREAMM-8: deeper responses with BPd vs. PVd

The response rate was almost similar between the two arms. However, the quality of response was much better with BPd versus PVd. So CR or better was 40% versus 16% and VGPR or better 64% versus 38% in the two arms, respectively.

Next slide please.

Slide 23 | DREAMM-8: higher MRD negativity rates with BPd vs. PVd

The MRD negativity was much higher, almost 7 times better or 5 times better with BPd versus PVd. The CR negativity MRD rate was 24% versus 5% in the PVD, and the VGPR MRD negativity rate 32% versus 5% for the two arms, respectively.

Next slide please.

Slide 24 | DREAMM-8: positive OS trend favouring BPd vs. PVd

The overall survival showed a trend in favour of BPd with a 12-monthprobability of survival of 83% versus 76% in PVD, and of course, the data are not matured yet.

Next slide please.

Slide 25 | DREAMM-7: changes in BCVA

How about ocular adverse events, which is the most important side effect, and I would say one of the very few side effects of belantamab? You can see that we are talking about the worsening of best corrected visual acuity because this is something that can impact the daily activity of the patients.

And you can see that 20-50 best corrected visual acuity reduction happened with 34% of the patients versus only 2% who had 20-200 or worse. The time to onset for the first event was 73 and 105 days, respectively. And the improvement of the first event happened in 98% and 100% of the patients, respectively. First event result in 94% and 80% of the two groups of the side effects respectively.

Next slide please.

Slide 26 | DREAMM-7: impact of dose modifications on PFS and ocular management

The median time between the doses increased the longer patients were in treatment and the dose delays did not have any impact on the PFS, BVd patients with at least one dose delay of more than 12 weeks, the median PFS was exactly 36.6 months. 23% of the patients experienced 20 to 50 or worse events in the first three months and the prevalence decreased thereafter as you can see in the graph. Rate of treatment discontinuation due to ocular events were very low.

Next slide please.

Slide 27 | DREAMM-8: bilateral worsening in best corrected visual activity

In the DREAMM-8, the respective number of patients with best-corrected visual acuity reduction to 20 to 50 to 20 to 200 were at 34% and 1% respectively. The first event resolved to normal baseline happened in 84% and 50% of the patients, but you can recognize that it was only one out of the two patients in the 20 to 200 group and the first event improved in 92% in all patients respectively. So visual acuity change that could affect activities of daily living were reversible in most patients for both studies.

Next slide please.

Slide 28 | Blenrep efficacy data is potentially transformation vs 2L+ SoC triplets

So in summary, we can say that in DREAMM-7, the combination of belantamab, Velcade and dexamethasone was 36.6 months compared to 13.4 months in patients who received daratumumab, Velcade and the dexamethasone after a median follow-up of 28 months.
The PFS was consistent across subgroups associated with poor prognosis, including patients with lenalidomide refractory or high risk cytogenetics.

We have a strong and clinically meaningful overall survival and more quality overall response rate, and durability of response with BVd.

In the DREAMM-8 study the medium PFS has not been brisk yet with the belantamab, pomalidomide, and dexamethasone versus pomalidomide, Velcade and dexamethasone, which the median was 12.7 months after a median follow up of 22 months. All of the patients in this study who had been exposed to lenalidomide and the PFS consistent across all pre-specified subgroups, including patients with high-risk cytogenetics or lenalidomide or anti-CD38 refractory patients who had greater response rates including MRD negativity with belantamab PomDex versus PVd and with an early signal for overall survival advantage.

Regarding safety and tolerability of BVd and bela PomDex regimen in the DREAMM-7 andDREAMM-8 studies, this was consistent with the known safety profile of the individual agents, with those modifications that were effective in enabling patients with ocular adverse event to achieve PFS outcomes and low treatment discontinuation rates consistent with that of the overall study population.

Next slide please.

Slide 29 | Study of BRd in 1L MM evaluates optimal dosing and dosing schedules

This study gave us the rationale to go to a Phase I/II study in the newly diagnosed patients who are not eligible for transplant. And these patients were intermediate fit or frail. We randomised the patients to receive either 1.4 milligram, 1.9 milligram or 2.5 milligram per kilogram, but given every eight weeks or every two months in combination with lenalidomide and dexamethasone and the primary endpoint was the safety, tolerability and the dose that we are going to go for the Phase II study and secondary endpoints included a lot of data, as you can see here.

Next slide please.

Slide 30 | Clinical activity observed across doses with no disease progression to date

The overall response rate was 100% in all the subgroups, and we've seen that we had a slightly higher number of patients with complete response in the Cohort 1 of the 2.5 milligram per kilogram, but who've very good responses in the two others – two other arms also. And the progression-free survival was extremely good as non-patients after a median follow up of 24.8 months has progressed.

However, we've had some deaths because the study was run specially at the time of the delta strain of SARS-CoV-2. That's why we have four patients who died because of COVID-19, and also about two patients who died because of pneumonia, one because of intracranial hemorrhage and one sudden death. Don't forget that these patients were intermediate fit or frail and the median age is 74 year of age.

Next slide please.

Slide 31 | Low frequency of ≥GR3 OAEs and meaningful BCVA decline were observed

Regarding the ocular adverse events, you can see that the vast majority of the patients had no Grade 1 adverse events, and the Grade 3 or more adverse events happened in very low number of patients. As you can see, for example keratopathy was for the Cohort 2 of the 1.9 milligram per kilogram every eight weeks, which was the dose that we have chosen to go to the Part 2 of the study was only 0.3%.

Importantly the time to resolution of keratopathy was only one month. The time to resolution of the best corrected visual acuity change from baseline was almost two months in all three groups and the time to resolution of meaningful BCVA decline was more than 3 lines drop in better seeing eye was between 1 and 1.5 months. The frequency in clinically relevant visual impairments happened in 10% in Cohort 1 with more than or equal to 3 lines drop in the better seeing eye to up to 13.4% in Cohort 1 and 7.7% in Cohort 3.

Next slide please.

Slide 32 | Ocular symptoms had minimal impact on activities of daily living

Regarding ocular symptoms who have impact on the activities of daily living and you can see in the second part of the figure, you can see that in the group of patients who received 1.9 milligram per kilogram every eight weeks who had only 5.7% of the patients who had almost most or half of the time symptoms that impair their clinical – their daily activity of living, while the93% of the patients had not such symptoms.

Next slide please.

Slide 33 | Appropriate belamaf dose administration critical to avoiding ocular events

And in order to achieve that, we had a schedule of, as we call it, appropriate belantamab dose administration. So, if you see within a red colour B, which we call it inappropriate belantamab administration is when the substantial ocular symptoms are present. And this can impact the quality of life of the patient and the daily living of the patient.

So, if we don't give belantamab at that time, then we avoid these side effects. And well, in the contrary, as you can see on the left, we will have an appropriate dose administration who have a dramatic reduction in the visual acuity. On the contrary, if you see on the right, the appropriate dose administration diminished the visual acuity reduction based on this initial chart.

Next slide please.

Slide 34 | Summary of BRd in 1L multiple myeloma

So, in summary, the extension of belantamab doses to every 8 weeks or even 12weeks if you had any symptom, did not lead to reduced efficacy compared to previous study implemented in the every three weeks schedule. This is also that the efficacy of belantamab is maintained even when administered in extending time intervals, as we've seen also in theDREAMM-8 study.

Furthermore, the extended dosing schedule had only minimal impact on vision related functioning with all or most of the day of the time in the activity of daily living responses recording less than 2.5% of assessments. Furthermore, the frequency of clinically relevant impairment in vision was low as meaningful BCVA decline was observed in less than 10% of assessment with a rapid time to resolution.

So thank you so much for your attention, and we are going to the next presentation now.

Luke | *Blenrep*

Slide 35 | Eye-related side effects experienced on Blenrep can be manageable

Thank you, Dr. Terpos. We greatly appreciate your time and expertise in sharing the potentially transformative DREAMM-7 and DREAMM-8 2L data, as well as insights from your clinical experience with your 1L data.

As you just showed that management of eye-related side effects is important to help patients achieve desired outcomes, so we are just going to have a patient here who has experienced and managed eye-related side effects while on *Blenrep* treatment.

Slide 36, please.

(video plays)

Slide 36 | *Blenrep* may have potential to improve upon standard of care in 2L MM

So, with the information you just heard from Dr. Terpos and the patient who has recieved *Blenrep* treatment, you can get a sense that *Blenrep* has the potential to meet unmet needs in 2L multiple myeloma.

Across both standard and heavily pre-treated populations, you can see on this chart provides information for each regimen regarding lenalidomide exposure, PFS within the ITT population, regimen constraints and frequency of administration. For both the standard and heavily pre-treated populations in 2L multiple myeloma, the *Blenrep* triplet regimens have the greatest (or equal) lenalidomide-exposure associated with the greatest PFS benefit and most convenient frequency of administration.

It is anticipated that *Blenrep* in both academic and community settings will be differentiating among the anti-BCMA class. We expect filings in all major markets by the end of this year.

Please turn to Slide 36.

Slide 37 | *Blenrep* may have a role in all patient segments and sites of care in 2L MM

Given the complexity of the multiple myeloma market, patient treatment eligibility can be broadly mapped along a scale of age and fitness, from young/fit to old/frail. On the left hand side of the chart you can see site of care breakdowns, which are listed across current standard of care as well as future anti-BCMA agents.

With the benefit-risk profile of *Blenrep*, it is anticipated that *Blenrep* would serve patients regardless of age and fitness levels, as well as being available in both academic and community settings.

It is this confidence in this broad applicability has given us the insight to further our *Blenrep* development programme in earlier settings, which Tony will discuss on the next slide.

Tony | *Blenrep*

Slide 38 | Multiple datasets support opportunity for *Blenrep* in 1L (NDMM)

Thank you, Luke.

We have just discussed Dr. Terpos's data in 1L multiple myeloma, and data from DREAMM-7 and DREAMM-8 that show *Blenrep* combinations that outperformed daratumumab. These compelling data and broad potential patient eligibility support our investment decision to initiate DREAMM-10, a Ph3 study of *Blenrep* in 1L multiple myeloma.
Please turn to the next slide.

Tony | *Ojjaara*

Slide 39 | *Ojjaara/ Omjjara* (momelotinib)

Now, moving to Ojjaara, which was recently approved for the treatment of myelofibrosis with anaemia.

Please turn to slide 40.

Slide 40 | Myelofibrosis patients with anemia have poor OS and limited options

Myelofibrosis patients experience disease hallmarks of splenomegaly, constitutional symptoms, anaemia and thrombocytopenia. Nearly all patients become anaemic over time, with worsening of anaemia associated with decreased overall survival.

1 year after diagnosis, around 50% of patients require red blood cell transfusion that severely impacts their quality of life. These patients need treatments that extend overall survival and address the spectrum of myelofibrosis manifestations.

Ojjaara is the only JAK inhibitor to address symptoms, spleen response and anaemia, and Luke will share us the recent launch success.

Luke | *Ojjaara*

Slide 41 | Strong *Ojjaara* launch uptake; establishing share in 1L and 2L settings

Now following the acquisition of Sierra Oncology in 2022, we accelerated commercialisation and launched *Ojjaara/Ojjaara* in the US and EU with line-agnostic labels. *Ojjaara* performance has been outstanding, I'm very pleased to say, delivering the fastest US launch uptake by a JAK inhibitor in myelofibrosis over the first two quarters post-launch. US share has been significant across both 1L and 2L with market research indicating ~60% of US HCPs indicating anticipated increased use within the next 6 months.

EU launches have also been successful in the UK and Germany, and Japanese approval is anticipated in the second half of 2024.

We are also exploring further indications of the overlap of oncology and inflammation with this target, and we continue to believe in the blockbuster potential of *Ojjaara*.

Please turn to slide 42.

Luke | *Zejula*

Slide 42 | Continued impact on ovarian cancer outcomes and promising data in glioblastoma

We're now going to talk about *Zejula* and the impact in ovarian cancer outcomes and promising new data in glioblastoma, which we're very excited about.

Next slide, please.

Slide 43 | *Zejula* development is mainly focused within ovarian cancer and GBM

Zejula is another one of our key medicines and continues to deliver sustained growth in 1LM setting in ovarian, and we've been able to more than double sales over the last 5 years in a very competitive environment.

Active surveillance in 1LM ovarian cancer remains high, despite evidence supporting use of PARP inhibition in this setting, particularly within the BRCAwt subpopulation who respond well to chemotherapy.

Additionally, alongside anticipated readouts in endometrial (RUBY 2) and NSCLC (COSTAR Lung), *Zejula* is also being explored in unmethylated MGMT glioblastoma, in which no meaningful treatment improvement has been seen in over 40 years. Clearly this is very important because with a high unmet need, which is indicated by an alarming 2% 5-yr survival rate for glioblastoma patients, *Zejula* the properties and potential to demonstrate meaningful improvement.

Tony will now take you through new data on slide 44.

Tony | *Zejula*

Slide 44 | Promising data in glioblastoma is a compelling opportunity

Thanks, Luke.

Zejula has a differentiated opportunity in glioblastoma. Unlike other PARP inhibitors, *Zejula* crosses the blood-brain barrier in pre-clinical studies, indicating favourable brain tumour penetration. Phase 2 data just presented at ASCO show promising improvement in a single arm study, which showed approximately a 15 month median PFS vs. 5 months historical standard of care.

These data give us confidence to imminently initiate a Phase 3 supported collaborative study with the Ivy Brain Institute in newly diagnosed unmethylated MGMT glioblastoma.

Zejula will be studied against temozolomide as the standard of care. Study primary completion is anticipated in 2027.

Luke | Immuno-oncology

Slide 45 | Immuno-oncology: Jemperli (dostarlimab) & CD226 axis assets

Next we will cover *Jemperli* and the CD226 axis slide, so can we go to that slide, please.

Slide 46 | *Jemperli* development is focused across endometrial, CRC and HNSCC

While *Jemperli*'s strong foundation is anchored in dMMR endometrial cancer, it is also being explored in colorectal and head & neck cancers.

Immuno-oncology has shown transformative outcomes for dMMR endometrial patients, while significant unmet need still remains for MMRp patients subgroup. In colorectal cancer, chemotherapy as the standard of care significantly impact patients' quality of life. So new treatment options are needed to deliver greater clinical benefit, and dMMR stratification is of clinical significance.

For head and neck cancer, clinical improvement is also needed and has not been seen in >20 years in the locally advanced setting. While ~85% of patients are PD-L1 positive, the benefit of anti-PD-(L)1 therapeutic has not been seen in early-stage disease.

The development of *Jemperli* across endometrial, colorectal and head and neck gives us confidence on the potential of this product.

If we move to Slide 47, please.

Slide 47 | *Jemperli* & chemo showed significant OS benefit in 1L endometrial cancer

Jemperli's foundation is in 1L dMMR endometrial cancer. In 1L dMMR endometrial cancer, the statistically significant PFS benefit in the dMMR/MSI-H population of the RUBY trial was not reached at 30 monts vs. 7.7 months of SOC – this is what led to US and EU approval in 2023.

If we look on a revenue sense, *Jemperli* has delivered >250% growth YoY (2023 vs. 2024) driven by unprecedented data coupled with strong execution on the ground. If we look at the uptake of *Jemperli* it has achieved about 33% new patient share in the US and >35% new patient share in Germany, with a strong UK performance since the launch in March of this year .

Building upon 1L dMMR success, the RUBY 1 trial is the only trial to show statistically significant OS in an all-comer population with 44.8 months mOS vs. 28.2 months. The 1L indication for all-comers in endometrial has been accepted for FDA priority review with an August PDUFA date. GSK will also be imminently filing with the EMA.

The impressive data for *Jemperli* gives further confidence in the future combination potential of *Jemperli* and our B7-H4 ADC in endometrial cancer. *Jemperli* is also being developed in other dMMR tumours, and Tony will walk you through our plans on slide 48.

Tony | Immuno-oncology

Slide 48 | *Jemperli* has shown transformative data in LA dMMR rectal cancer

Jemperli has indeed been shown to have clinical benefit in other dMMR-driven tumours, such as rectal cancer. Recent ASCO data from a supported collaborative study with Dr Cercek from MSK show unprecedented 100% complete clinical response in the 42 patients treated with *Jemperli* monotherapy. These responses are durable with no evidence of progression.

Data from this study provide continued confidence in our AZUR program in colorectal cancer. AZUR-1 explores *Jemperli* monotherapy in a locally advanced, unresected setting for dMMR rectal cancer. The study's designed to inform if *Jemperli* monotherapy could potentially replace chemo and surgery as standard of care.

AZUR-2 explores *Jemperli* monotherapy in a perioperative setting for dMMR colon cancer. This study design also lends to *Jemperli* potentially replacing chemo as standard of care. Data from

AZUR-1 and AZUR-2 are expected beyond 2026 contributing to the >£2bn asset ambition for *Jemperli*.

Let's hear more from Dr. Cercek on the unprecedented findings serving as the foundation for *Jemperli* development in colorectal cancer.

(video plays)

Slide 49 | *Jemperli* development is focused across endometrial, CRC and HNSCC
These are truly impressive data, and we hope that patients continue to benefit from *Jemperli* monotherapy.

Slide 50 | *Jemperli* being explored in locally advanced head and neck cancer
Beyond dMMR tumours, *Jemperli* is also being investigated in locally advanced head and neck cancer.

JADE 3 is a Phase 3 trial that builds on development lessons in head and neck cancer and explores *Jemperli* monotherapy as a new standard of care in a post-chemoradiotherapy setting. Two notable trial design elements are important here: 1) selection of a specific newly diagnosed, treatment-naïve patient population, and 2) a post-cisplatin-based CRT setting, allowing optimal potential for PD-(L)1 benefit.

Slide 51 | GSK and iTeos have started the Ph3 GALAXIES Lung-301 study in NSCLC
Jemperli is additionally being studied in non-small cell lung cancer combination with belrestotug. The Phase 3 programme spend for belrestotug was gated and dependent upon preliminary interim efficacy and safety data from the Phase 2 GALAXIES study.

Consistent with the recent iTeos disclosure, interim analysis from this study found that the combination of *Jemperli* and belrestotug exceeded pre-defined efficacy criteria, with clinically meaningful tumor reduction at each dose. Data also indicated an acceptable safety profile. We expect to present these data in 2H 2024.

As such, GSK and iTeos will imminently initiate the Phase 3 GALAXIES Lung-301 study in previously untreated, PD-L1 high current/former smokers with locally advanced, unresectable or metastatic non-small cell lung cancer.

This is the first registrational study for the belrestotug-*Jemperli* combination.
Several elements provide confidence in belrestotug in this competitive setting. These are the molecules optimised Fc engagement, greater potency, clinically proven Treg depletion and the proven anti-PD-1 profile of dostarlimab as evidenced in the PERLA trial.

Please turn slide 52.

Slide 52 | *Jemperli* development programme explores monotherapy and combinations

In summary, our *Jemperli* development program spans multiple solid tumours as either monotherapy or as a combination backbone where we envisage differentiated outcomes relative to the class.

We are confident in *Jemperli* as an IO backbone and will develop *Jemperli* proprietary combinations across our portfolio.

Moving now to ADCs on the next slide.

Slide 53 | Antibody-drug conjugates (GSK5733584 (B7-H4), GSK5764227 (B7-H3))

Next slide, please.

Slide 54 | GSK5733584 (B7-H4 ADC) builds on presence in gynaecologic cancers

GSK'584 is our ADC with best-in-class potential in gynaecologic malignancies.
B7-H4 protein is highly expressed across these malignancies and serves as a key immune checkpoint.

Hansoh presented clinical data at ESMO in 2023, showing an ORR of 33% and 27% at two different doses in triple-negative breast cancer patients in China for this molecule. GSK will develop '584 in novel combinations with proof-of-concept studies initiating later this year.

Please turn to the next slide.

Slide 55 | GSK5764227 (B7-H3) has multi-indication, transformational potential

GSK'227, targeting B7-H3, is our second in-licensed ADC from Hansoh. Antigen expression is broad across numerous tumours with high unmet need and presents exciting development opportunities.

Clinical activity disclosed at ASCO 2023 in small cell lung cancer patients, shows a 63.6% ORR for this molecule. This broad clinical activity provides confidence in monotherapy use in relapsed/refractory disease, as well as combinations in earlier settings, particularly with dostarlimab. We believe that '227 has the potential to be first-to-market in several tumours.

Now handing back to Luke to conclude on slide 56.

Luke | Future ambition

Slide 56 | Delivering upon our future ambition

Next slide, please.

Slide 57 | Delivering upon our future ambition

To conclude, this slide shows peak sales potential for key assets and the material contribution oncology can have to GSK even before we add - we hope - the relaunch of *Blenrep*. *Ojjaara* continues to deliver strong performance, with physicians indicating a switch to *Ojjaara* treatment within the next 6 months. We'll continue with geographic expansion in the near-term.

Jemperli is a critical backbone of our immuno-oncology development programmes. Further growth in endometrial cancer with pending regulatory decisions and development beyond dMMR-driven tumours will drive growth.

belrestotug (TIGIT inhibitor), nelistotug (CD96 inhibitor) and our PVRIG inhibitor can also contribute with doublet and triplet combinations focused in NSCLC and HNSCC. We will also initiate GSK sponsored clinical trials for our two ADCs, GSK'227 (targeting B7-H3) and GSK'584 (targeting B7-H4). Our clinical development programmes will combine each ADC with proprietary combinations with enormous potential.

Finally, Dr Terpos walked us through impactful *Blenrep* data to showcase this important medicine and its potential to benefit patients significantly. We have excluded *Blenrep* from our long-term ambitions, but it clearly represents a significant upside opportunity for us, and we look forward keeping you updated on the progress of this asset.

Turning to the last slide.

Slide 58 | Delivering upon our future ambition

As a reminder, here are the forthcoming catalysts that you should monitor to track our progress Overall, we are very confident in delivering across our three core disease areas: haematology, gynaecologic cancers and emerging tumour types – whether through antibody-drug conjugates, immunotherapy or targeted small molecule modalities – these medicines will significantly contribute to the delivery of our long-term ambition and continued momentum.

So with that, thank you and we will go back to Nick, and we will open it up to Q&A.

Q&A

Mark Purcell (Morgan Stanley): Thank you very much, Nick, and thank you for hosting the meeting. I have just two questions. First, can you help us understand the competitive landscape for BCMA-targeted medicines? There are a number of other approaches out there, which I guess you highlight in the slides, but if you can compare any other ADCs in development but also CAR-Ts, bispecifics, etc., and provide some colour as to where *Blenrep* sits relative to those?

Secondly, as far as the greater than £3 billion peak sales potential un-risk-adjusted for *Blenrep*, can you help us understand how significant the second-line setting in isolation is relative to the first line ambitions? Thanks very much.

Luke Miels: Thanks, Mark, and good afternoon. On the first question - if we can go to Nina to cover the competitive landscape and I'll comment on the £3 billion-plus ambition.

Dr Nina Mojas: I am just checking whether you can hear me okay? [*Yes*] I will start and I will probably ask Dr Terpos, who is also on the call, to add his perspective.
From the landscape perspective, I think this is something that we need to continue to remind people. For US specific, the majority of the patients - about 70% of all patients - are treated in the community setting, and this is relevant to your question, Mark, about comparing to other BCMA agents.

If we look at bispecifics and particularly CAR-Ts, these are agents or assets that are administered in the hospital setting largely in the academic centres, both because of the administration but also because of the management of adverse events. That addresses the first part of the question about how does it compete. Keep in mind community setting, it is the community physicians who like to keep their patients: these are second-line relapse patients who do not prefer to spend a significant amount of time in hospital and, particularly, are not very keen on managing those adverse events, delivering the drugs or supportive care that requires hospitalisation. That is just on the convenience.

On the efficacy, we have seen the data for CAR-Ts and in the second-line setting for bispecifics, we still haven't seen the data in second-line, so we will need to see where it goes. But, comparing the efficacy of *Blenrep* versus CAR-Ts, we are actually not too far. Then once we see the bispecifics, we will see if the efficacy that they deliver will be worth the process of hospital administration, significant infection risk and management of other adverse events that, again, requires hospitalisation. I don't know if Dr Terpos wants to add something from his own experience?

Dr Evangelos Terpos: The anti-BCMA treatment seems to be the fourth pillar of multiple myeloma therapy and for patients who have been exposed to both daratumumab and lenalidomide upfront, which is the vast majority of patients in both the US and Europe, we can say that in second-line we do not have a lot of available options. For example, if we talk about what is available for now - not off-label of course - in Europe for a patient who progresses on daratumumab and lenalidomide in the MAIA regimen, you can see that the only reimbursed regimens include the old-fashioned PomVD, SVD and KD and only in a very few countries, including in my opinion only Germany, and with specifications in Switzerland and Austria, cilta-cel can be given. Therefore, I think we have an unmet need here and the two studies, especially that of the belantamab with pomalidomide and dexamethasone seems to cover this unmet need.

Just to let you know that especially in Europe, the cilta-cel is available for the vast minority of the patients who are eligible to receive it, even in countries like Germany that is the most in use country of cilta-cel in Europe and from what I have heard, the vast majority of patients also in the United States do not have the possibility to have the CAR-T because they are treated outside of academic centres.

This is one thing, but on the other hand even if you see the efficacy, as Nina mentioned of the belantamab and you compare it with the cilta-cel which is the second-line option that can be given to the patients, it's not far away.

On the other hand, it is much more convenient, it can be given to intermediate fit and frail patients that definitely is the majority of patients with myeloma but not to forget what is the median age of myeloma at diagnosis. In our centre, for example, it's 69 years. In other countries it's 71 or 72, so the standard myeloma patient at first relapse is not the patient that we see several times in clinical studies, so definitely is not 62 years of age or 64 years of age. It is much, let's say more elderly and not eligible for receiving CAR-T in the vast majority of cases, not only because of age but mainly because of comorbidities and frailty.

I believe that both combinations will give the opportunity to our patients to have very good therapies. Bela Vd has given the best efficacy in patients who have been exposed and are refractory to lenalidomide and also bela-Pom-Dex to me offers special attention for patients who have been given daratumumab and lenalidomide, especially those who are refractory to one or both of these agents.

I don't say anything about the bias because I want to talk about evidence. I am one of the authors of the guidelines of EHA for example for the treatment in myeloma, so I want to talk only based on evidence. We have no data at all for the patients for one to three lines of prior therapy with bispecific studies in BCMA, although I have to say that from some of the data that are

reported during ASCO and EHA for first-line therapy, it seems not to be, to me, extremely encouraging, especially for the side effects, the safety profile and especially the infection rate.

Luke Miels: Thanks, Dr Terpos and Mark, I'll just cover your second question very quickly. Look, I think you should see that £3 billion-plus that we communicated a couple of years ago as a base. The bulk of that is the second-line setting and I think what is hopefully becoming very clear to you from the experience that Dr Terpos has discussed and Nina's answer, after the analogue that we are looking at is CD38 Darzalex in that second-line setting, so you can start to model the scale there. Of course it is always subject to regulatory interactions and the ultimate first-line design that we go through.

James Gordon (JP Morgan): Hello, thanks for taking my two questions. The first question was *Blenrep* and I just noted you reintroduced a peak sales forecast but it isn't yet part of the guidance, even though the guidance does include some assets that are quite a lot earlier. Why is that or when might you have the confidence to add it back in? Is it that you still need more mature OS from DREAMM-8 or more tolerability or something like that? Why are you being a bit more cautious than some of the other assets where you seem to have quite a lot less data that seem less de-risked?

And the second question was are you in competition from other approaches? Clearly bullish on the TIGIT but how does this compare to other approaches, both your own and competitor approaches? I know for instance you have a TIM-3 that reports next year that wasn't on the guide or your catalyst list. There are also other people doing TIGITs, not just monotherapies, but like bispecific or even bispecific TIGITs combined with TROP-2 ADCs, so could it be that TIGIT's a good approach, but actually a bispecific approach is better or even combining a bispecific with a TROP-2 ADC could be even more efficacious?

Luke Miels: Sure, James, thanks. On the first question … have a few more regulatory interactions but I hope you get the sense of the amount of time that we have allocated, the thoughtfulness that we have spent around how to manage the benefit-risk of *Blenrep*, so we will update in the future, all in good time.
Hesham, maybe if you could cover James's second question, please.

Dr Hesham Abdullah: Yes, happy to do that and James, thank you very much for the thoughtful question. I think probably first and foremost it is important to highlight that we have a number of different immuno-oncology assets that we are currently evaluating or assessing across different

tumour types and you touched on of course TIGIT but also dostarlimab which is our PD-1 inhibitor and then of course TIM-3, cobolimab as well.

With that in mind, I would also like to highlight that there are two other assets in that CD226 axis beyond TIGIT which includes CD96 but also of course our PVRIG as well. With that in mind, what I would like to highlight is for TIGIT when compared to other assets, it is a bit more unique. Of course it is FC-enabled, that's one. Two, we are actually looking at of course in this instance, combining it with a PD-1 inhibitor, dostarlimab, which we have actually benchmarked quite well to other leading PD-1s in the class.

You may recall of course we had the Phase II data from the PERLA study. This was a head-to-head study of dostarlimab plus chemotherapy versus pembro plus chemotherapy in first-line non-small cell lung cancer and it actually demonstrated what appeared to be similar levels of clinical activity in the context of response rates, but also encouraging trends for p-secondary endpoints that include progression free survival and overall survival as well, two of the data was previously presented at ESMO most recently in 2023. With that in mind as well too, we feel that of course having this TIGIT that is FC-enabled, a really strong PD-1 backbone, and then of course some preliminary data that is emerging from our Phase II platform study, where we've actually looked to explore different dose levels of TIGIT, specifically three different dose levels as well too, relative to the benchmark of a PD-1 inhibitor, our own dostarlimab, which again has performed consistently as pembrolizumab certainly, at least at this stage the data is encouraging, it warrants us moving forward with a Phase III investment.

Beyond that we are also thinking more holistically across our portfolio. You may have heard from the presentation that we also have access now to our own B7-H3 antibody-drug conjugate. B7-H3 is expressed in non-small cell lung cancer and we expect to actually be evaluating that as a part of different combination regimens. So you talked about the role TROP-2 ADCs may have to play in lung, I think B7-H3 will also be a key asset in that capacity as well too. We'll actually be looking to combine it with our TIGIT and our PD-1 inhibitor as well, looking at that relative to for example, what other competitors may be considering and evaluating as well.

TIM-3, we are really positioning of course in this post-IO setting, so we have our ongoing Phase III study which is called COSTAR, looking at the combination of dostarlimab plus cobolimab plus docetaxel, versus docetaxel plus dostarlimab, versus docetaxel, it's a three-arm study. It initially began as a Phase II/III trial graduated from Phase II into to Phase III, based on some pre-specified thresholds for clinical activity that were met on certain key surrogate endpoints and the Phase III study is currently ongoing.

Again, you may be aware of course that TIM-3 in expressed in non-small cell lung cancer and certainly as a key primary resistance mechanism to checkpoint blockade and specifically PD-1. So, we think the rationale makes sense from that perspective and we know the study graduated from Phase II to Phase III because it met some of the key, at least, efficacy criteria at that time point. So, all in all, what I would say is we are looking at different ways to at least evaluate and assess a number of different agents that we have across our portfolio, they include different IO assets. They include sequencing, they include combinations with other therapeutic modalities, such as antibody drug conjugates and may include potentially looking at earlier stages of disease, again, all based on data as it continues to emerge and outcomes as well at that point in time.

Luke Miels: Thanks Hesham, I think James, you have seen with the approach in TIGIT internally that we are very disciplined - and Hesham made this point several times - very disciplined in terms of looking at clinical profile and the evidence before moving, but when we do make a decision to move, we are going to move in a very focused way, but we are going to move with speed when we see what we like.

Matt Weston (UBS): Thanks very much. Two questions please. The first is on DREAMM-10 and now based on the readout using MRD, approximately when would you expect we'll see a readout of that trial. And then my second question is to Dr Terpos and it's about sequencing of drugs. So we now have some great data from *Blenrep* in second-line from DREAMM-7 and DREAMM-8 and now the proposal is to take *Blenrep* into the frontline, but really we have no idea what to do with a *Blenrep* patient after it's been used in the frontline setting. So as a clinician I would be really interested as to whether or not, if it were positive in frontline, you would be prepared to use the drug not knowing what to use next, or whether really we should wait for overall survival data from DREAMM-10 before we can really understand the sequencing benefit of *Blenrep* in the earliest lines?

Dr Evangelos Terpos: Matt you are right, that if a BCMA agent especially belantamab is approved in the first-line, we don't know exactly what will be the sequencing, but what we discussed previously was exactly what is happening in the treatment of myeloma, all the drugs are approved in that way. They are going first to one thousand per cent unmet need which is the very end of myeloma then they go to the early relapses, one, two, three lines of therapy and then they go to first-line. What we are talking about today we are talking for patients who are refractory to daratumamab first-line, and the options that I offered, or at least the options that are offered to physicians, include, outside of the US, mainly PomVD, the OPTIMISMM study, that included no patient who had been exposed, not only refracted, but had been exposed to dara;

SVd, I think there were 11 patients who had been exposed to dara in the SVd arm; KD, no patient had been exposed to dara, and of course, we have also the cilta-cel that has now been approved, and includes mainly lenalidomide refractory patients and very few who were exposed to dara.

So it is difficult, and now we are having the first, let's say, very good regimen, like bela-Pom-dex, which to me, it would be the second-line therapy outside of cilta-cel when it's going to be available, and is going to be for a minority of my patients, bela-Pom-dex which is going to be for these patients, and there are data for these specific patients.

So unfortunately, it's the same with all the drugs. You see that the T-cell engagers were licensed in the very end myeloma after the fourth-line of therapy, and now we are having studies in first-line. So what's going to happen next after them? We will be obliged to have either the older regimens, dara or isatuximab-based therapies, or the CAR-Ts, or the bispecifics, while we know, for example, the CAR-Ts are not doing so well after BCMA, but this happens at the very end. Or we do the same if we give belantamab upfront, using it every two or three months, and then to give cilta-cel second-line. We don't know if the results will be similar to belantamab in two-class refractory patients and cilta-cel after.

So, your question is extremely important, but I don't think there will be any physicians who can give you an answer because, unfortunately, what you described is exactly what we are facing in our clinical practice where all the drugs are first approved in the very late myeloma, and then go slowly to one to three prior lines of therapy, and then to first-line. At the time they are approved at first-line, the available options at second-line, all these data, are based on studies which have not had any patients who have been exposed to the drug that is now in first-line.

I have tried to answer your question. I know how difficult it is. We don't have any data. The data that we have in the very end-stage myeloma, I don't think that they will be confirmed in the first or second-line. Then every time we need to create new data for what's happening with the specific combination after a new approved indication.

Dr Hesham Abdullah: If it's okay, just to touch on what Dr Terpos was highlighting in the question early on – should we wait for survival data before we start moving drugs into front-line.

What's interesting is probably, as we look at the existing data for CAR-Ts in second-line, we haven't necessarily seen either of the CAR-Ts actually demonstrate a statistically significant improvement in overall survival. What we have seen, at least in DREAMM-7, is a very narrow miss to demonstrate stat-sig OS at the time of the interim PFS analysis which was positive, of course. The narrow miss was by .00012, and so we feel very confident that at the time of the next pre-

specified interim OS analysis for DREAMM-7, we will be able to demonstrate a stat-sig OS benefit. That's the first point.

The second, of course for DREAMM-8, you see the hazard ratio is 0.77. I expect that to get better over time, especially given the duration of response that this drug can demonstrate, *Blenrep*, that is, and so with more maturity of data, and more follow-up, I think you'll see that change over time as well.

Getting back to the question around DREAMM-10, I think everyone is well aware, of course, that there has been a recent Advisory Committee meeting that was held and convened by the FDA in the US, whereby there was overwhelming support of course for the adoption and the use of MRD negativity as a surrogate endpoint in multiple myeloma. With that in mind, and with the data and the meta-analysis that were generated on the correlation of MRD to long-term outcomes, we are planning on incorporating this as a co-primary/dual primary endpoint in DREAMM-10, so both MRD negativity and, as well, PFS.

I think I would probably also call everyone's attention to the data that Dr Terpos presented during the presentation, which actually showed, at least in both DREAMM-7 and DREAMM-8, in DREAMM-7 more than a twofold increase in MRD negativity rates, and then in DREAMM-8, actually a fivefold increase in MRD negativity rates. That certainly gives us a lot of confidence, hope as we think about DREAMM-10 and the potential for demonstrating that type of improvement.

Now, again, I would just like to highlight two things. One is, we are going to continue of course to progress with our current filing plans globally, for the second-line indications, including DREAMM-7 and 8. As Luke alluded to in the presentation, those filings are planned for the second half of this year, and we will have filed in all major market regions by the end of the year as well. Of course, we have been in ongoing dialogue with health authorities, regulators and we will continue to give at least additional updates as we move into the latter part of this year. That will certainly also continue to support our evaluation, our assessment of DREAMM-10.

In terms of timings for MRD negativity and when it could potentially read-out, again, these are all of course time-to-event and types of endpoints and it will really depend on the extent of follow-up but what I would say is maybe there is a range in Europe and the possibility of two and half to three years that we could be looking at, so by late 2027 or 2028, but again we have to look at and assess and evaluate where the thresholds are set for demonstrating a meaningful improvement in MRD negativity.

Peter Verdult (Citi): Thanks. Just a few questions, please. Just a follow-on on Matt's question about timelines. I think at ASCO you said three years, so we are looking probably at a launch of '28, '29. Can you remind us the IP situation on *Blenrep*, given the false start we have had so far? When do you expect or what is the GSK view of the timelines in terms of major LOEs?

And then just to Dr Terpos, and maybe the GSK team themselves, the discussants at ASCO were almost saying less is more and urging the company to almost explore lower doses, given how durable responses have been and although you have ameliorated the ocular tox, it's still bothersome. I would be interested in Dr Terpos's view about exploring longer dosing intervals, lower doses still, whether you have an appetite to do that at GSK.

And then one cheeky follow-up just for Tony on the ADCs. It was clearly a massive theme at ASCO. There are now hundreds in development. BH-74 and -73 are clearly hot targets – every man, woman and dog seems to have one, so can you help just triangulate for us whether you feel you are in the vanguard on these ADC targets or the rear guard? Are there any indications where GSK could be first to market? Thank you.

Luke Miels: Thanks, Pete. I'll answer your first question very quickly, so 2032 for the primary patent in the US [with potential data exclusivity extension to Aug 2034]. Dr Terpos, if we could turn to you and then once you have concluded, Tony, I will hand it over to you.

Dr Evangelos Terpos: Thank you. I think what you mentioned is what I have investigated. In the first-line therapy as you have seen my study in combination with lenalidomide and dexamethasone, I checked lower doses like 1.4 and 1.9mg/kg given every eight weeks. The standard dose of 2.5mg/kg is given every eight weeks, so we start with that and we have now 66 patients with a median follow-up of more than 24 months. I can tell you that we have had only one progression and the majority, if not all the patients, if I am correct now, all the patients are receiving now 1.9mg/kg every 12 weeks, so every three months and the efficacy is extremely good. All patients have responded to treatment.

Of course we talk about newly diagnosed patients but I have to tell you that all my patients in this study have intermediate fit or frail according to the IMWG frailty score, so they are patients that are not the fit ones, so we have had extremely good results suggesting that the drug is very well tolerated. The ocular problems that we have with this schedule is very low and the efficacy is very high.

I think that based on some of the preliminary data that I had, GSK used a different schedule in DREAMM-8, to me it was extremely important, starting from the higher dose, 2.5mg/kg and then to 1.9mg/kg after the second cycle, so they lowered immediately the dose and they gave it every

four weeks instead of every three weeks in the DREAM-7 because they recognised early that the efficacy probably is the same giving the drug every four weeks or even every eight weeks, because a good number of patients – I am not in a position to say how many of them – in the DREAMM-8 are in the every eight-week schedule and the efficacy is very good.

I believe that it is a very efficacious drug. One thing also that has not been published yet but I can tell you from the analysis that we have seen, is that the higher the dose, the higher the ocular toxicity, the higher probably the response rate. So I think for the relapsed/refractory setting I like this schedule of starting with the 2.5mg/kg and then to immediately go and lower the dose to 1.9mg/kg every four weeks and then to go to the 1.9mg/kg every eight weeks, if the patient has ocular toxicity.

I believe that, Peter, you are right, that in the real world I believe that the majority of the relapsed/refractory patients are going to have after an initial dose, will be having the drug every eight weeks for example if it is with Pom-dex or every six weeks if it is with Velcade and dexamethasone. In the real world the drug is going to be given every two or three months offering very good results to these patients.

Dr Tony Wood: Thank you. Just a sort of headline; as far as the two ADCs are concerned, I'd say in the context of H-4 very much competitive and in the leading pack. For H-3, as Luke mentioned earlier, what we are focusing on there is generating differentiated data through the platform studies. Then when we have those data in hand moving aggressively and quickly, recognising the competitive environment. A couple of things to stress on top of that, obviously it's unlikely these agents will be administered in the context of regimen outside of immunotherapy and we are very competitive in the PD-1 and TIGIT spaces as you have already heard, and having individual assets which will allow dose titration to achieve optimal effects as well as potentially optimised profiles and across the growing position and understanding of *Jemperli* as a backbone therapy, not only in gynaecological cancers, but in lung.

Probably the other thing to emphasise since you asked the question of me, of course we will continue to allocate capital across the portfolio in terms of the principles that you've heard before from Luke and myself, that's very much focusing on our return on investment and the potential to drive long-term growth. So I think we are great shape, we are certainly in a good position and the decisions we will take will be on the basis of differentiated data in the context of platform and building out on the strength of position we have in gynaecological cancers.

Luke Miels: Hesham did you want to add?

Dr Hesham Abdullah: Just a quick build on what Tony highlighted as well. I think first and foremost, I would just highlight that one of the elements of course that's really important of course for antibody drug conjugates is really not only the target but the linker and the payload and one of the things that we have done at least in terms of looking at B7-H3 and B7-H4 is evaluate and assess our belief in the behaviour of the platform itself, that we have access to now through Hansoh, and we believe that it behaves very consistently with the leading platforms and the likes of Daiichi-Sankyo, so that's one.

Two, actually combinations. Combinations are going to be really important they are going to be very critical for the development of these types of ADCs, and certainly that includes combinations with in-house assets like dostarlimab, PD-1, combinations with other targeted therapies that may synergise with the topoisomerase warhead. Those might include other agents that target DNA damage response. And then three of course, existing standard of care.

Then three, I would say we have built capabilities, we have recruited a lot of great talent that has had experience with antibody drug conjugates, whether it be Daiichi whether it be at AstraZeneca, or other certainly big biopharma but then also moving with pace. Moving with pace and continuing to assess any potential opportunities as they emerge.
Then finally what I would say is, strategy matters. I think everyone recalls of course what happened with the PD-1 PD-L1 class, it wasn't always about being first and it's the right strategy, the right development strategy, the right tumour types, the right combinations, the right approach and the right patient segments and biomarkers that will be really critical to the success of antibody drug conjugates. So I just want to highlight that and then just say, stay tuned. For anyone that knows me, knows I do try to note things and then you guys can look at them in hindsight and reflect on whether or not I was right or wrong.

Luke Miels: Thanks Hesham. I need to say some days when I come to work I think I might have walked into my old Swiss employer or another UK company where I spent some time, but I think, critically, we have been able to assemble a group of people on the back of this collection of products as Hesham has said, that have a track record of picking opportunities and there's a recognition that operating in oncology is different.
Again, the theme of focused discipline and speed and that balance is something that we are very quick to emphasise and again, it's just the tip of the iceberg with the people that you see on the call today in terms of the people that we have been able to assemble to support these assets, so that's very exciting. Shall we go to the next question Nick, please.

Dr Tony Wood: One very quick comment to cap off on Hesham's point that we have also built significant manufacturing capability associated with *Blenrep* and that's going to be an important aspect of indication expansion in this area.

Luke Miels: Absolutely, thanks Tony.

Emmanuel Papadakis (Deutsche Bank): Thanks for taking the question, a question on *Blenrep*, thinking about the sophisticated complexity of Dr Terpos' answer on the dosing algorithm, one of the virtues of *Blenrep's* applicability is its ease of use in the community setting, presumably, you need a well defined dosing algorithm to avoid community doctors getting lost on complexities and worrying about trading off efficacy over safety? So if DREAMM-7 and DREAMM-8 are approved what are you expecting to be labelled in terms of how they manage dose levels and frequency? Then in DREAMM-10, what are you planning to actually use as the dosing regimen? And a quick one on *Ojjaara* you don't seem to have any additional clinical development plans, are you planning or considering a BET-combination study, how much of an impact do you think that's going to have on the treatment landscape in the frontline if that combination is approved? Thank you.

Luke Miels: Thanks, Emmanuel. If we can cover the expected label and there is probably a linked question to that that will come up, which is pricing. One of the positives of withdrawal is that we can reset pricing in the US and Europe, so we will need to think through that, but it's a nice problem to have. Hesham, over to you for dosing, expectant label.

Dr Hesham Abdullah: Thank you very much, Luke. Emmanuel, a good question and what I would start out with and say is that I think what we have probably seen at least from some of the additional analyses that we continue to generate is it is really important to start with the 2.5mg dose, so that is really important and critical, especially in the context of the second-line setting where patients are coming in, they have existing disease and getting that depth of response early on for the first one to two cycles is quite important.

With that in mind, I think everyone is well aware of course that the drug was used at 2.5mg every three weeks schedule at least per protocol, within both studies, so that will be probably the starting point, but there are also toxicity management guidelines that were implemented in each study as well. We are hoping of course that at least as we engage the regulators and we share the data of course within our submission that being able to manage each individual patient based on those toxicity management guidelines and using the dose reductions, the interruptions as a means of guidance will be important. This is not new.

It's not new to *Blenrep*, it's not new in oncology, it has been done across multiple assets before, where you dose each individual patient based on their level of tolerability to the drug and you use, of course, the side effects that they are experiencing, as a means of actually titrating the dose down, delaying it and so forth. So again, based on some of the data that we are seeing within the study, and you probably saw it from the patient as well, dosing at every six weeks, dosing at every eight weeks, those are things certainly, again guided by the individual patient experience, are things to think about or consider in that context.

Luke Miels: Thanks, Hesham. And Nina, if you could just cover the LCM thoughts for *Ojjaara* quickly and then we will go to the next question.

Dr Nina Mojas: Yes, definitely. When we licensed the asset, we actually had some plans for combination therapies and combination assets that had been in development in myelofibrosis. Unfortunately, for the last ten years it has been a graveyard of drug development and many of those potential partners fell off, so navitoclax is not a candidate anymore. We still have to see what is going to happen with the BET inhibitor with pelabresib; is this going to cross the regulatory line or not? If it does, there potentially is a space for the combination because both ruxolitinib and pelabresib are myelo-suppressive, so potentially causing even more anaemia and thrombocytopaenia than the individual agents on their own and momelotinib would be a very good combination partner, but we first need to see what happens with pelabresib.
Beyond myelofibrosis, we are looking at additional indications where momelotinib could have a very interesting role and mode of action would fit that gap, but we will announce once we initiate those studies, we will start talking about it at that point.

Luke Miels: Super, thanks, Nina.

Graham Parry (Bank of America): Great, thanks for taking the questions. A quick question on DREAMM-10; it looks from the slide that that is powered for superiority. I just wondered, is there a non-inferiority test in the design there or is that just going to be a straight shoot-out where you need to show superiority?

And then secondly, just regarding the opportunity for *Blenrep*, most KOL feedback has been that they would prefer CAR-T, if it is available in a large treatment centre, but to your point, 70% of patients are out in the community setting, so could you just talk there to the practical management of liaising with ophthalmologists for managing the eye toxicity?

And within that setting, do you still think it's going to be more frail patients that would be getting this, so perhaps just help narrow down that target population even more, roughly what percentage of the second-line myeloma patients are we talking about there?
Thank you.

Luke Miels: Thanks, Graham. Hesham, if you could please take the DREAMM-10 and then Nina, you have done a lot of work in terms of the pathways in the US and then Graham, if I could just build on your question and ask Dr Terpos at the end; if you had a patient in front of you that you were looking to initiate on this treatment and they raised ocular complications with you, how would you explain that in layman's language to that individual around your treatment strategy and how you are going to manage that?

Hesham, you first, then Nina and then if we could ask Dr Terpos.

Dr Hesham Abdullah: I am happy to, thank you, Luke. First and foremost, just in terms of what the potential design of DREAMM-10 could look like from a statistical analysis perspective, I would just start off by saying it has been great to see of course the emergence of a number of different therapeutic modalities recently in multiple myeloma for patients. That is important and we have to acknowledge that, just in terms of providing treatment options.
But with that in mind, in order to continue to move the field forward, we have to also take into account that we need to provide at least potential therapeutic options that actually provide patients with a step-change in treatment outcomes and the potential for better therapeutic benefits. If anything, the DREAMM-10 study design will be certainly looking at, or focussing on, demonstrating superiority to an existing standard of care regimen in front-line in multiple myeloma.

I think the DREAMM-7 data gave us a lot of confidence in that. I think if you look at all of the different outcomes in the study, whether it be the primary outcome of the study PFS, with a median over a little over 36 months, versus 13 months on the daratumumab based arm. If you look at the key secondary outcomes, duration of response, depth of response and certainly also of course overall survival, which is still preliminary at this point in time, they all give us a lot of confidence in what the DREAMM-10 outcome could look like, but more specifically of course, in demonstrating superiority in that regard.

We have to certainly acknowledge that as you look at the number of different at least existing therapeutic modalities that are available to patients that target BCMA, some have limitations, in terms of their side effect profile. We have talked about of course the CAR-Ts, the potential for risk of early death, especially with bridging therapies and so forth and there is even an advisory committee meeting that was held around that for both assets. We see the infection rates, Nina

spoke to those as well too with bispecifics, both of course require hospitalisation and they are not available to patients in the community setting.
That's actually where 70-80% of multiple myeloma patients go and hence that's where the unmet need currently exists as well too, and of course that's beyond what Tony highlighted around the investments that we are making in manufacturing, where we have of course CAR-Ts limited by manufacturing and supply chain challenges as well too.

The other piece I just want to touch on was actually around the patient populations and the types of patients. Dr Terpos will touch on this better than I can of course, but I would just like to highlight that we have seen at ASCO data on sub-groups presented from DREAMM-7 and DREAMM-8, so if we wanted to talk about how this drug works or in which sub-groups of patients this drug works, actually it works in everyone. Thankfully it's able to provide a meaningful benefit to patients that are high risk, patients that are standard risk, patients with extra medullary disease. Patients that have received prior lenalidomide, lenalidomide refractory. Patients that have received prior dara and DREAMM-8 as well too and I think that's really important. There was one slide that Luke presented during the presentation that shows which types of patients *Blenrep* would actually be good for and certainly what you could see is all types of second-line patients, irrespective of number of prior lines of therapy, irrespective of risk and irrespective of fitness as well too.

Dr Nina Mojas: So very briefly, a lot will really depend on the label and the REMS or no REMS requirements. If you remember our first *Blenrep* launch in the US, the REMS requirement was quite stringent and challenging, definitely. So what will be the requirement in the end will determine to which extent and how physicians, haematologists need to engage with the eye care professional. Is it going to be ophthalmologists specifically, or it's going to be potentially optometrists. How frequently and for how many infusions that interaction needs to happen, all of that will be quite critical and will determine how much of an effort a physician will need to go through to initiate patient successfully.

What we do know in the meantime, because now we are talking after having hundreds and thousands of patients treated versus three or four years ago when we launched when it was dozens of patients treated, is what we know is no patient went blind, no patient lost their eyes, no patient died because of ocular adverse events, unlike many of the other therapies that you are talking about. What we do know also is that many physicians, after treating more than one patient, they start to recognise how to treat the patients and they start to be able to manage those ocular eye related side effects on their own. I am not sure that there is anyone better to describe it than Dr Terpos, who has a lot of experience with that, so I will ask him to also answer the question.

Dr Evangelos Terpos: Thank you. I think you touched now on one of the most important aspects of belantamab I believe that the ocular toxicity, although as Nina mentioned, is something that cannot kill you, or nobody was blinded because of belantamab mafodotin, it is a toxicity that may create some problems, only when the patient hears that you may have some eye problems. When you have a patient in front of you, because that was the question, you have to explain to him what he has to expect from belantamab, not only the efficacy of course, that we know, it's very easy to understand but also of the safety and the ocular problems are not so severe in the majority of the patients. The majority of the patients may have a gritty eye, a sore eye maybe some pain sometimes, but I mainly focus on the number of patients that may have a problem in their daily activities. If the patient cannot read, cannot see their tablet or smartphone, cannot drive or they have problems in seeing television, especially at night, these are real important problems.

That's why one of my main intentions is to manage, to make the drug ophthalmology-free, let's say, if possible, and in order to do that, in our study, we have the randomisation between the reduction and the handling of the drug based only in the ophthalmology assessment, and in Group B, we have both the ophthalmology assessment and the OSDI questionnaire, but the first five questions describe symptoms while the other four describe activities of daily living, like reading, watching television or reading a tablet and smartphone or driving.

I can tell you that in the dose that we used in the newly diagnosed multiple myeloma patients with the 1.9mg/kg every eight weeks, there was less than 5% of more than four hours' - as we say - during the last five days of problems in daily activities. This is the time that you have to stop the drug and then to restart when this has totally recovered.

I want to tell you that we have several patients with the ophthalmology Grade 2 keratopathy and they have almost no problems at all. Until now, according to this evaluation, we had to reduce or to stop the drug administration.

I believe that very soon, we will be in the position that we can say that, for the vast majority of the physicians, possibly for one, two or three cycles at the most, we may have an ophthalmology evaluation because the physician needs to be secure with what they are doing, and then, based on the questionnaire, we are going to provide a very good tool, the anamnestic tool, in order to drive the decisions.

Don't forget that, initially, we had bortezomib, for example, many years before with the peripheral neuropathy, we gave it twice per week, and then we ended up with once per week, and the patients had the electromyograms and everything going to neurologists for the peripheral neuropathy. Now, of course, this peripheral neuropathy is very well managed by the

haematologist, and I believe one of my tasks is also to provide the tool for the haematologist in order not to need the ophthalmologist, or at least to need the ophthalmologist very rarely.

One more thing that I want to focus on is, seeing now more than 300 patients on belantamab, especially the newly diagnosed patients, we have seen that there is ophthalmological problems in a very high frequency in these patients. I talk about newly diagnosed because someone can tell you that their relapsed refractory patients have received probably a lot of dexamethasone that creates these problems. The main problem is cataracts. Initially, I have seen that almost all my patients – and in the elderly patients – have cataracts in the study, and I wanted to check, let's say, the incidence of cataracts in healthy individuals. We have seen that in above the age of 70, between 65-75%, in the majority of the epidemiological studies. The cataract is a problem. Why is it a problem? With keratopathy Grade 1, if you have cataract Grade 1 or 2, you may have no problems, no blurred vision, nothing, but if you have keratopathy Grade 1 and a cataract Grade 3 and 4, then you may have blurred vision and reduction in your vision acuity.

I think this is something we have to take into consideration when we talk about ophthalmological toxicity. The toxicity that *Blenrep* is creating is reversible in more than 90% of patients within one month of treatment. That is why giving the drug every eight weeks, for example, or even every six weeks after the initial dose, then you can have very good results.

Another important issue is what we are doing in our study in the newly diagnosed – but I haven't seen it yet in DREAMM-7 and 8. When we describe the number of patients that have an event, especially an ocular adverse event, then, even if the patient had a keratopathy of Grade 2 or 3, let's say, during the first cycle, and never in the future, then this is described as one event.

I would like to see what we are having in our newly diagnosed studies, the number of ophthalmology visits with problems. Then you can realise that the number of patients who continue to have a problem, probably after one event, may be zero afterwards, or it may be extremely less.

In order to conclude, I believe that we have ophthalmology toxicity of belantamab mafodotin, which is totally manageable, is totally reversible, very fast. That's why the administration every six to eight weeks is extremely easy to do. One of my tasks now is to provide an anamnestic tool to the physicians in order to make them ophthalmology-free, and I believe that we will make it and we will transform belantamab, like bortezomib, that the physicians can do it after some time, of course, that they do all the reductions and alterations in the administration of the drug by themselves.

Luke Miels: Fantastic! Thanks, Dr Terpos. I think a very practical outline on something that is going to be utilised by community-based physicians.

Navid Malik (TLSD): Thank you; a quick couple of questions. On *Zejula*, in unmethylated MGMT-GBM patients, can you tell us in the Phase II study how many IDH1 mutations there were in treatment versus the historical control? I am kind of intrigued as to why you are not necessarily looking right now anyway at the MGMT methylated patients who could be evaluated in a separate trial.

And the second question on *Blenrep*. For intermittent and low dosing, although I don't think this is seen right now, but is there a possibility you could introduce some degree of resistance or refractory elements because you are obviously not giving the dose in a consistent way – you are taking the patients off once they receive these ocular side effects?

Luke Miels: Sure, thanks, Navid. I think on the *Zejula* unmethylated population, Hesham, if you could cover that, and then Dr Terpos, if we can just come back to you in terms of your thoughts on this resistance question.

Dr Hesham Abdullah: Let me start off first just about going after the unmethylated patient population, and specifically of course, I think everyone is well aware that this is an area of key unmet medical need, and typically outcomes tend to be even worse in terms of prognosis, so why did we evaluate this patient population? That's really a reason of course that Dr Sanai [Director, Ivy Brain Tumor Center] and I had actually assessed them in their study, so that's one.

Two, I think probably also just highlight that the IDH mutations are typically of quite low prevalence even in GBM as well, so with that in mind, we can certainly look into how many patients there may have been but I expect there to be very few, if any, that were part of this cohort that was treated in the investigator-sponsored trial as well.

One thing to just highlight specifically regarding your second question around resistance of course, and Dr Terpos will probably touch on this a little bit. As of now at least and based on the data that currently exists in the field, we are not necessarily seeing that there is any BCMA antigen loss that is happening. Actually that is not the case and what I would also highlight is the discontinuation rate actually due to the eye-related side effects is actually rather low in both DREAMM-7 and 8, so it's actually less than 10% in both studies as well, so it's not necessarily why

the patients are coming off treatment, but Dr Terpos can certainly touch on the resistance question.

Dr Evangelos Terpos: The resistance to BCMA seems to be extremely interesting. In general, the resistance has two important pathways. The one pathway is the reduction in the BCMA expression in the surface of the plasma cells that we believe was the main, but it seems that this is not the main and the critical point of the resistance. The critical point seems to be the BCMA, let's say the change in the form of the BCMA, in the surface of the myeloma cell in order that the antibody cannot bind to its binding position, so there is a mutation there that makes the antibody not to bind in its position and that's why we have the resistance. And this is not only with the belantamab, it is with teclistamab, with elranatamab. It has been shown, especially by the work of Nizar Bahlis from Calgary, several times.

I don't think that if you give the drug every six or every eight months this is going to increase the resistance. On the contrary, even the clinical data suggests that this happened as the majority of the patients will have let's say a bigger interval between the administration, they would have worse results which is not happening.

That's also when you go from the one anti-BCMA agent to the other, the other can work. That's why I don't believe that it is the lower expression of the BCMA that makes the difference.

Probably the mutation status is what creates the difference and that's why probably after belantamab another anti-BCMA-based regimen, for example, teclistamab may work as we have seen that it can work at a lower rate of response of course, but it can work.

I don't believe that if we give the drug at intervals of six or eight weeks this will create any problems in the refractoriness of the disease, so this isn't the resistance to that, it may be even the opposite.

Luke Miels: Thank you. Okay, I think we are up to the last question which is Peter Welford.

Peter Welford (Jefferies): Thanks for fitting me in. I have two quick ones. First, coming back to the DREAMM-10 design, I notice you say about possible standard of care. I am curious to know your thoughts - and I imagine you have not yet determined this - as to what the standard of care would be. I guess the most relevant, is Darzalex potentially being considered, i.e. a second antibody base, or will this most definitely not be combined with the Darzalex regimen in the first-line.

Secondly, coming to the TIGIT, you have talked about the interim analysis triggering the 'go' decision to Phase III and being very disciplined on this. I wonder if you can give us a bit more insight as to whether, first, is it based on response rates, or do you have any measure of long-term follow-up as far as duration of response and then early survival curves in the Phase II?

With regard to the toxicity, I believe there are some in the field who have seen incremental toxicity when they are combining the two IO agents. If you can make any comment at all on what you are seeing with regard to the tolerability of your *Jemperli*/belrestotug to date, that would be great, thank you.

Dr Hesham Abdullah: I will start with the first question about the choice of the control arm regimen and DREAMM-10. As I touched on earlier, we are planning on looking at or evaluating what is a CD38-based regimen in front-line as a control arm. For example, you have the MAIA study, which included DRd, but you also look at some of the recent data that have been emerging including data from the IMROZ study with isatuximab as well. Again, I would say there are different patient populations. We know that the triplet versus the quadruplet-based approach has different trade-offs, at least for such a control arm, with regard to potential toxicity as well. However, I would say we are definitely going to be looking at a CD38-based regimen and, based on the DREAMM-7 data, you can get a sense that a dara-based regimen, at least for a sponsored GSK study, would potentially be a key one to consider as a control arm.

That is not to say we wouldn't evaluate, at least through other mechanisms, generating data with quadruplets or generating data that compares us to quadruplets. That is also an option that we will consider, evaluate and assess.

To your second question around TIGIT and the preliminary data we have used from an interim analysis from our ongoing randomised platform study, I would say it is a combination of different surrogates that we are evaluating and assessing. Of course, the data continue to mature over time, but it is certainly looking at a combination of response rates, also looking at preliminary duration of response data but also depth of response through molecular response and circulating tumour DNA data. Therefore, it is a combination of all three and, again, we shall continue to follow those data over time as they mature.

I would just highlight that we anticipate presenting those data at a future scientific congress. To note, at least for the Phase III study, we have appropriate gating criteria that we have built into it to make sure that we continually assess the data that are emerging from the platform trial relative to any measures that we have included in the Phase III study.

Luke Miels: Thanks, Hesham. With that, we will conclude. I think if you look at this from a specialist perspective or a generalist perspective, the sense of progress that we are making in this very focused and disciplined fashion hopefully is apparent and justified your time today in joining us, and the team behind this collection of assets. I would also like to thank Dr Terpos for joining us today out of his busy schedule; we are very grateful for the time you have taken to inform people with an interest in the company. Thank you to everyone who joined today and we appreciate the thoughtfulness of your questions and the time.

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