Post-ASH Blenrep Investor Call
Tuesday, 10 December 2024 at 4pm GMT / 11am EST

Introduction | Jeff McLaughlin

Welcome to this GSK Investor Science Call, following data presented on *Blenrep* at the 2024 American Society of Haematology annual meeting. The slides we are presenting now are also posted in the Investor section of gsk.com

Slide 2 | Cautionary statement regarding forward-looking statements

On slide 2, you will see our usual cautionary statement.

I will now hand the call over to Luke Miels. Luke.

Luke Miels

Slide 3 | Today's Agenda and Speakers

Thanks, Jeff. Hello, and thank you for joining our update today on *Blenrep*. With me today we have Dr Paul Richardson from the Dana-Farber Cancer Institute; Nina Mojas, from Global Product Strategy; Hesham Abdulla, Global Oncology, and Mondher Mahjoubi, our Chief Patient Officer.

Today, we will take you through a brief strategic overview of our Oncology business; then the DREAMM-7 overall survival data presented at ASH yesterday and the likely practical application of *Blenrep* in clinical practice. We will also provide some additional context for how we might position *Blenrep* within second-line multiple myeloma and finally we will take you through why we have confidence in our plans to now develop *Blenrep* for use in a first line setting.

Next slide please, Jeff

Slide 4 | Multiple Oncology approvals in the next 3-5 years, expanding into a range of solid tumours with significant unmet need

Before we get into the detail, a few words on our Oncology business, which is evolving rapidly, generating £1 billion of sales in the first nine months of the year – more than double last year. Strategically, our current focus is in haematological and gynaecological cancers, with marketed assets *Ojjaara*, *Zejula* and *Jemperli*, and *Blenrep* now filed for approval for the treatment of second-line multiple myeloma. Looking forward, we are expanding our focus into additional solid tumour types, including lung, colorectal and head and neck, with both B7-H3 ADC and *Jemperli*.

I would also like to say that business development will follow the pattern executed to date and, driving all of this, we are prioritising R&D capital investment into Oncology, to accelerate the development of assets with the greatest potential, as you would expect, like *Blenrep*, the ADCs and *Jemperli*, but we have also implemented effective stage-gating and checkpoints to ensure disciplined, optimal but timely and competitive investment decisions.

Next slide, please.

Slide 5 | Blenrep summary

As you may have seen in yesterday's presentation, DREAMM-7 has demonstrated statistically significant and clinically meaningful improvement in the overall survival, with the risk of death in relapsed or refractory multiple myeloma reduced by 42% with the *Blenrep* combination versus daratumumab-containing standard of care. These data support our 7 completed regulatory filings, including in the US, where we expect a decision by the end of July next year.

During today's call, we will describe how *Blenrep* has the potential to transform treatments for both patients and physicians across both community and the academic settings. And, why the strength of the data in second line and early data in newly diagnosed patients provide us with the confidence to initiate the development programme in first-line multiple myeloma.

Next slide, please.

Slide 6 | DREAMM-7OS Update

Now, thanks to Dr. Paul Richardson, who will kindly take us through the DREAMM-7 OS update as well as his perspectives on the relevance of this drug in clinical practice. Over to you, Dr. Richardson

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DREAMM-7 OS update | Paul G. Richardson

Thank you very much, Luke. It is a real privilege to be here and I am very grateful to Nina and everyone in the team for helping me to get here on time. Thank you. It has been a very busy and exciting meeting but it is so good to see that belantamab is back in a very dramatic fashion. It was wonderful to see the presentation yesterday from Vania Hungria.

Slide 7 | Blenrep multimodal mechanism of action

I just want to walk people through the mechanism, just to give some way of introduction to those folks on the call about how the antibody drug conjugate platform works and why we are so frankly excited by belantamab, and have been obviously for some time, recognising the challenges a year or so ago. Really the results of both DREAMM-7 and DREAMM-8 coming through, as we've always believed, to demonstrate the true value of belantamab in the setting of relapsed refractory myeloma.

Just a quick background point to make. Obviously this is a targeted strategy, targeting BCMA with a payload that not only induces direct apoptosis within the myeloma sub, but critically it is profoundly immunogenic, and I think that's incredibly important to appreciate because this probably in part explains why it is so successful in combination. I think the other point to emphasis is obviously there is a very, I think, elegant engineering to have ADC effects which obviously results in an effector cell activation, which is very important to its mechanism as well. But from our point of view, the immunogenic signal is particularly attractive because it explains some of the synergy that we see, with both protease inhibition which in itself has immunogenic cell death as part of its mechanism, and indeed its power with the IMIDs and looking to the future and with other drugs such as CeLMoDs, it really does make sense that there is a bright future for belantamab.

You may say why and I'll just quickly say in short, the other highlights of the meeting, we're really recognising some of the challenges of the bispecifics, particularly infectious risks which we don't see with belantamab, and also some of the real challenges, albeit rare, but nonetheless very importantly because they appear to be highly toxic and potentially even fatal in the CAR-T space. This could not be more timely in my opinion to bring in a new strategy to target BCMA that is clearly in my opinion safer in the broader sense. The other piece that is so

important to appreciate is the ocular toxicity is really better understood and can now manage, and in combination it allows us to dose belantamab that much less frequently, and by so doing, the ocular toxicity has become really manageable.

On the other hand also, and literally in my own practice, I have never seen it not be reversible. It's always been reversible, and the data now support that.

Slide 8 | DREAMM-7: Study design and endpoints

Anyway, to get on to the presentation of DREAMM-7, which Vania did so nicely, thank you. As people are aware, in terms of the eligibility criteria, patients had to have had one prior line of therapy, and obviously had progressed after their first line, prior therapy with an anti-BCMA strategy was not permitted, and obviously they could not be refractory into the control platform which was daratumumab or to bortezomib which was the key partner with both dara and belantamab.

I think what was very courageous in DREAMM-7 was to really take dara head on and basically it was a combination of belantamab/bortezomib/dexamethasone, leveraging this synergy that was seen in earlier phase studies in the DREAMM programme, and then comparing it to a standard of care that we all considered to be a powerful standard of care, not one that is in any sense second tier, and that is daratumumab/bortezomib/dexamethasone. Obviously beyond the first eight cycles, maintenance was provided with either belantamab monotherapy which I think is an important point here, or daratumumab monotherapy.

The primary endpoint was PFS. Key secondary endpoints were both overall survival and duration of response, and MRD negativity, or the assessment of MRD status, was a key correlative.

Slide 9 | Baseline characteristics and prior treatments received were balanced across both arms

In terms of the characteristics of the patients, obviously this was a well-sized adequately powered trial, about 500 patients strong. As you can see, our oldest patient in each arm was either 86 for the triplet, belantamab/bortezomib/dexamethasone, and 89 for DaraVd, with a median age of 65 broadly across both arms, a slight preponderance of male sex which is typical for myeloma.

Then what I think is particularly interesting is the high-risk population were well represented, almost a third. What is also very important to note is that these patients were in large measure heavily exposed to immunomodulatory drugs, and in particular to lenalidomide, and in fact about a third were refractory to lenalidomide, which is an area of unmet medical need. I think this was important.

What is also critical to understand is that prior proteasome exposure was permitted, but obviously patients could not be refractory and/or intolerant to it.

Slide 10 | BVd nearly tripled median PFS vs DVd (36.6 vs 13.4 months)

So, what did we see. First and foremost to share with you the PFS benefit was quite striking. As you can see, the median PFS for the bortezomib/belantamab mafodotin arm plus dexamethasone was striking 36.6 months and for the daratumumab/bortezomib/dex arm, what one would expect at 13.4 months, so there was no evidence on this control arm that it was performing anything other than actually slightly better than we had seen in other trials, but what was particularly striking is that essentially a more than doubling of PFS benefit.

Obviously the hazard ratio here was remarkable at 0.41, and this was highly statistically significant.

Slide 11 | BVd had an early, sustained, and statistically significant Overall Survival benefit vs DVd

I think this is the real meat of the presentation to you folks this morning. This, I think, was remarkable to all of us. What we see here is that there was an early and sustained and highly clinically meaningful overall survival benefit for the belantamab/bortezomib/dexamethasone triplet, and as you can see, the median for BVd has not been reached. In fact, overall, but the hazard ratio is .58, and as you can see, if you do an estimate, I think this estimate was particularly important to understand the implications of these Kaplan-Meier curves. The predicted median OS based on modelling was remarkable at 84 months for the triplet, compared to 51 months for DVd. You are seeing basically a 33-month gain in median overall survival.

For all of us in the myeloma community, this was profiled as the top abstract at the International Myeloma Working Group meeting on Saturday morning, and I think with very good reason. I think that reflects the international community in myeloma research's opinion on how important this finding is.

Slide 12 | Deeper responses reported with BVd vs DVd with statistically significant MRD(-) benefit

So what about the MRD? I think it's nice to see this. Obviously you may be very familiar that the FDA have taken a very favourable view of MRD as an important primary endpoint now that we can utilise it in clinical trials, and that's very welcome.

As you can see here, we saw not only a high-quality response rate advantage, the overall response rate for bortezomib/belantamab/dexamethasone was 83.1%, the control arm was 71%. Again, performing much as expected, but the difference here is for the belantamab-based therapy, we are seeing VGPR or better exceeding 65% and a CR rate or better of 36%.

Then if we pivot to the MRD-negative group, you can see here that there is over-doubling of MRD rate in favour of the belantamab/bortezomib/dexamethasone arm, and in fact if you look at the VGPR or better group, it's very, very interesting. It's 39% for those patients receiving the belantamab/bortezomib/dexamethasone triplet versus around 18% for DaraVd. So really interesting results and certainly supports the striking PFS and OS gain that we see.

Slide 13 | Duration of Response with BVd was more than double that of DVd

In terms of DoR, this again was particularly exciting. You can see here that the median DoR for the control group for daratumumab/bortezomib/dexamethasone was 18 months, very much as expected, and again this control group, I would argue, performed slightly better than we saw in prior trials. What I think is particularly important, though, is the median DoR for the belantamab platform is a striking 41 months, which, from a patient perspective, is tremendously important.

This obviously was exciting, but what was also very important is that there was no penalty in what we call PFS2. In other words, by deploying belantamab/bortezomib/dexamethasone early in relapse, patients didn't lose on the backside of that, and the PFS2 favoured belantamab with a hazard ratio of .59.

Slide 14 | Eye-related side effects were manageable and reversible

What about the ocular side effects? I think it's very important to hear from us as clinicians as to what this means for our patients. This graphic is very helpful. I would like to focus on the 20/50 figure in the middle, because for those patients who do experience blurring of vision, that is typically what they may encounter.

The 20/200 on the far right we show just for completeness, but it is extremely rare, and in fact, if you look at the data, it supports exactly that. I think what is tremendously important is that the blurring of the vision is the

predominant ocular side effect. There is really minimal corneal irritation or pain, and in fact, with the use of appropriate eye drops and eye care, we have been able to manage this very well, and the critical aspect of management is the interval of dosing and the actual dose itself. By managing this proactively with ophthalmologists, we have been able to generate practice guidelines now that will make this a far easier platform for community oncologists to deploy. Our hope is that we will be able to minimise the need for ophthalmological specialists – I use that term broadly because in different healthcare jurisdictions, it's different – to be involved in using these practice guidelines.

As you can see from this trial, very reassuring in this regard, and of course it was a challenge, as expected. It is also important to note though, however, that obviously highly relevant was the reversibility of it, and what is critical is the discontinuation rate. In an international multi-centre setting, the discontinuation rate was just 10%, so I think that speaks volumes to the fact that this was manageable in the best sense of the word and I think what's also very important is this is very consistent with what's been seen in DREAMM-8 and other experiences across the DREAMM programme overall.

Slide 15 | Conclusions

So I think in conclusion we're very excited by these results for a very important reason. Belantamab/bortezomib/dexamethasone is in fact the only triplet combination to be compared directly to Dvd with a different MOA essentially as the platform and what you can see here is early sustained separation of overall survival, this translates clearly into a survival benefit with a hazard ratio of 0.58. I think what's really exciting is to give people an estimate based on really I think robust modelling that we have 84 months of belantamab/bortezomib/dexamethasone, versus 51 months for the control group. That translates to a 33-month difference in favour of belantamab and that's a median of course.

What's also important to share is the doubling of CR rates, the doubling of MRD negativity and the doubling of medium duration of response. So all of these parameters of clinical benefit, either they use surrogates or direct measures, are translating in the right direction with a positive clinical benefit effect seen.

I think the toxicity issues, whilst we deal with these eye related side effects, I am very happy to take questions on this, what's really important to share is we didn't see much else and the most important thing in my opinion is the absence of a serious infection signal. This is really important and discriminates I think belantamab very favourably and other BCMA targeting strategies, be they bispecific, or for that matter CAR-T. I think to my mind, clearly belantamab mafodotin now - and I've always felt this actually from the get-go - is a standard care for patients with relapsed disease and in my opinion provides a very important option in a real-world practice. I am very happy to take questions about what I mean about that going forward.

Slide 16 | Relevance for clinical practice

Now I realise were going to talk about relevance in clinical practice, so basically I will go through this, so perhaps it will head off some of the questions and if there are still questions obviously please feel free.

Slide 17 | Blenrep is highly efficacious option for 2L MM

I think a couple of context questions, there's a number of points to make. There is clearly this DREAMM-7 benefit which is so encouraging, but I think what's so important also is to share the DREAMM-8 experience as well, where this consistency of clinical benefit appears to be very real. And again, the depth and durability of response, as I have mentioned already, the doubling of DoR and of course the improvements in MRD negativity, now these are seen across both trials and very importantly the eye related side effects are reversible. So we will move through this carefully, because I think I have touched on a lot of this already to some extent, but it's worth emphasising this.

Slide 18 | DREAMM-7: High response rates maintained with Blenrep dosing extended to ~ **8-12 weeks**

Now, I think one point to share with you and this is a question that has come up during the meeting is, how are response rates maintained when you dose at extended intervals? Now this is very exciting and it's something we saw in DREAMM-1 and DREAMM-2 to be frank, that you could actually space out dosing and clinical benefit was sustained.

I'll never forget one of my patients in DREAMM-1 who enjoyed three years of remission after completing therapy so this was not an unusual affect in my opinion at all. It was certainly nice to see it validated in the Phase 3 clinical trials. So essentially what you could do is maintain response rate if you extended *Blenrep* dosing intervals to eight to 12 weeks. This data clearly shows that and similar trends were observed with the extended dosing in DREAMM-8.

I think that's a very important point from a practical aspect, because dosing frequency represents a low treatment burden therefore and I think it's therefore really, it's such a key point, that you're not therefore just limiting Belantamab mafodotin use to top academic centres in major urban areas, you are actually being able to really deploy this in community setting. I think this has tremendous relevance in US practice but above all actually also means that on a global scale we are providing patients with a real access to BCMA targeted therapy.

Slide 19 | Blenrep is highly efficacious option for all 2L MM patient segments

So I think in that context one can say the following comments, I think these are absolutely supported by the data, Belantamab mafodotin is highly efficacious and in a setting of second-line therapy. I think you can extend the intervals eight to 12 weeks. It's very interesting to share with you this so-called grade 3/4 toxicity question, because please note, this is bi-ocular ophthalmological assessment and it's all about microcyst density. What I think is very important to share with you from a patient perspective, you may see reports of Grade 3/4 based on microcyst density, actually for a patient, this can be quite different and they can report to you that their visual acuity is in fact remarkably better and actually to them, not without any obvious difference in baseline, but yet they will still have microcyst densities that would be scored as grade 3. I emphasise this point because, in practical terms, in my opinion this looks more concerning that it actually practically is from the patient's perspective, and so I think that is very important.

The other point to make is that we showed manageability and, as I mentioned, in our practice, we have not had a single case that has not been fully reversible.

Then what I think is particularly important as well is that this validates combination strategies with belantamab mafodotin across a variety of settings and not just in relapsed refractory disease – as obviously has now been clearly shown. We can start to realistically think about moving this upfront and we already have data from colleagues such as Dr Evangelos Terpos in Athens in Greece, which clearly shows it is not only feasible but highly active.

Above all – and this is so important, especially now everyone says that COVID is behind us, yes and no. The reality is that you don't need hospitalisations and this has implications not only in the context of infectious risk and all that that entails, but also from the point of view of resource utilisation. I think this is a very exciting time, with very exciting results to share with you today.

Positioning of Blenrep in RRMM | Nina Mojas

Brilliant. Thank you, Dr Richardson, for your presentation but also for all your insights from your real-world practice.

We are moving on now and I will address the question that we are asked frequently about the potential positioning of *Blenrep* in relapsed refractory multiple myeloma.

Next slide please.

Slide 21 |1st relapse in MM is a critical moment in evolving treatment landscape

The first relapse in multiple myeloma for most patients is the most challenging point in their patient journey: for many of them, as they communicate, it is more devastating than their initial diagnosis. The data on the left-hand side of the slide illustrates that, with each relapse, the likelihood of patients receiving the next line of therapy almost halves. These data clearly highlight the importance of using the most effective therapy as early as possible in their treatment, simply because the option to receive the therapy in the next line might not be there.

The treatment landscape in multiple myeloma is evolving. At this point, most of the patients in the first line receive lenalidomide and, increasingly, daratumumab is also being used, particularly after the results of the so-called MAIA study were published. We currently anticipated that around 70% of the patients in second- line have received lenalidomide in first-line, and around half of them are still daratumumab-naïve. These are the patients that were studied in DREAMM-7, where *Blenrep* demonstrated an overall survival, as we have just discussed.

In the future, we expect that the proportion of second-line patients who are daratumumab-naïve will decrease as the share of daratumumab-based regimens in first-line increases, and with greater use of daratumumab or other CD-38 antibodies, there is an increasing need for novel targets, such as BCMA-targeting agents like *Blenrep*.

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Slide 22 |Blenrep offers option with overall survival benefit and low treatment burden

There are a number of BCMA-targeted treatment options available or currently in development in the second-line setting, including *Blenrep*, CAR-Ts and bispecific antibodies. This slide outlines the most relevant characteristics of the three modalities. As you can see, each of these agents offer deep and durable responses but, so far, only CAR-T and *Blenrep* have shown a statistically significant overall survival benefit. We are still awaiting the update for bispecifics in second-line studies.

The safety profiles for each of these three modalities are very different. For bispecifics, the most prominent adverse events include cytokine release syndrome and infections, which may require sometimes repeated hospitalisations. Emerging evidence suggests that CAR-T therapy shows infrequent but irreversible adverse events, such as Parkinsonism and an increased risk of second primary malignancies. In contrast, data from Phase 3 studies with *Blenrep* show reversible and manageable eye-related side effects, of which the most frequent grade 3/4 events is blurred vision.

Around 70% of multiple myeloma patients are managed in the community, as Dr Richardson pointed out already, where simple treatment administration protocols are quite important in determining the choice of therapy. However, both bispecific antibodies and CAR-Ts require hospitalisations for the initial treatment and the management of adverse events. In contrast, *Blenrep* offers an off-the-shelf outpatient treatment with dosing

frequency potentially extending to 12 weeks or sometimes more, as indicated in both DREAMM-7 and DREAMM-8.

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Slide 23 |Blenrep as an option for patient segments across care settings in 2L MM

With the product profiles that we just saw, we do expect that CAR-T and bispecifics are going to be reserved largely for academic settings, where hospitalisation is readily available and then also for young and fit patients who are more likely to tolerate the associated procedures, but also the side effects. With the *Blenrep* profile we see an opportunity to be positioned across both community and academic settings and also is suitable for both young and fit, but also older and frail patients. And as we saw earlier in DREAMM-7 data, *Blenrep* has superior outcomes over daratumumab-based regimens and is therefore well positioned versus current standard of care which is still largely in second-line daratumumab-based based regimen.

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Slide 24 |Quantitative market research show strong momentum for anti-BCMA therapies and Blenrep

When we look at the market research and what it tells us, it indicates that there is a very strong growing preference for the use of anti-BCMA therapies across all lines of relapsed refractory multiple myeloma. On the right-hand side of the slide, the intent to prescribe data, demonstrates increasing confidence in *Blenrep*. As a reminder, this data was collected before this weeks' presentation of overall survival, even before the headline of the positive overall were announced and we do expect that this positive trend is going to continue, as we plan to launch *Blenrep* in the second half of 2025.

I am now going to hand over to Hesham, who will take us through the reasons to believe and future development plans for *Blenrep* in newly diagnosed multiple myeloma.

Development program in Newly Diagnosed Multiple Myeloma (NDMM) | Hesham Abdullah

Slide 26 |Ph1 DREAMM-9 Blenrep Quad (BVRd) in Transplant-Ineligible Newly Diagnosed Multiple Myeloma

Thank you Nina and as you have now heard from Dr Richardson, we have quite extensive experience across the *Blenrep* development program, evaluating *Blenrep* across over 1,700 patients treated to date in our sponsored studies and overall 7,000 patients have been on *Blenrep* treatment. We are now moving towards first-line, or newly diagnosed multiple myeloma study looking at both triplet and quadruplet combination regimens with *Blenrep*.

In the first-line patient population, it is important for us to identify alternative doses and schedules that deliver similar benefit, while continuing to further enhance tolerability of *Blenrep* based combination regimens. In DREAMM-9, we evaluated *Blenrep* in combination with VRd in newly diagnosed patients. We assessed doses ranging from 1-1.9mg/kg and a range of dosing intervals including dosing schedules ranging from 6-12 weeks to assess preliminary anti-tumour activity, along with eye related side effects.

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Slide 27 |Blenrep Quad achieved response of 100% at doses 1.4-1.9mg/kg and with schedules of 6-8 weeks

Importantly, we found that response rates remained high at doses between 1.4-1.9mg/kg and with schedules of 6-8 weeks. I want to draw your attention to two key points on this slide. First, we saw a 100% overall response rate in dose cohorts between 1.4-1.9mg/kg and with schedules of every 6-8 weeks. Second, the purple and yellow sections of the bar charts demonstrate CR and sCR rates of 62–92% in the first four cohorts.

Next slide please.

Slide 28 |High rates of MRD (-) achieved at doses 1.4-1.9mg/kg and with extended schedules of 6-8 weeks

Consistent with the depth of response rates observed in the prior slide, this slide shows high rates of MRD negativity achieved at doses between 1.4-1.9mg/kg and again with schedules of every six to eight weeks. You may have also noted from the data presentation earlier this weekend, dose cohorts with 1.4-1.9mg/kg achieved faster MRD negativity rates as well.

Next slide please.

Slide 29 |Preliminary DREAMM-9 Safety: Grade 3/4 event rates reduce with extended schedules

Based on recently published Phase 3 data with CD-38 targeting quadruplet regimens, the tolerability burden of quadruplet combinations is obviously very important. Across all dose cohorts with schedules ranging from every six weeks to every 12 weeks, the incidence of Grade 3/4 eye related side effects ranged from 3-18%, which compares quite favourably to rates that have been reported with Q3 schedules.

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Slide 30 |Blenrep quad could yield improved efficacy vs anti-CD38 quads in ALL NDMM patients, including high risk

It is also useful to put into context the preliminary data from the DREAMM-9 study against other key datasets in front-line multiple myeloma patients.

Obviously, the usual caveats and limitations of cross-trial comparisons apply here, especially as the DREAMM-9 data is preliminary and limited in sample size. However, early indications are favourable and give us additional confidence that *Blenrep*-based combinations could improve current standard of care in newly diagnosed multiple myeloma patients, given the higher and deeper responses observed.

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Slide 31 |In addition, Blenrep triplet in NDMM showed 100% ORR and no disease progression to date

We are also encouraged by data that Dr Terpos previously presented – and Dr Richardson had alluded to earlier – from this investigator sponsored study, which looked at the combination of a triplet of *Blenrep,* lenalidomide and dexamethasone in first-line patients, demonstrating an overall response rate of 100% across all dose cohorts and interval schedules investigated.

Next slide, please.

Slide 32 |Study design for Blenrep triplet in 1L (DREAMM-10)

This slide shows the design of our first Phase 3 first-line study, DREAMM-10, which will evaluate a triplet-based regimen of *Blenrep* with lenalidomide and dexamethasone versus daratumumab, lenalidomide and dexamethasone regimen. DREAMM-10 has a dual primary endpoint of MRD negativity and PFS and is expected to start recruitment imminently.

In addition, leveraging the results from DREAMM-09, we are currently in the process of assessing further late-stage trials, including quadruplet regimens to ensure *Blenrep* is appropriately positioned for different patient segments with newly diagnosed multiple myeloma.

Next slide, please.

Summary | Luke Miels

Thanks, Hesham, and thank you Dr Richardson and Nina. If we go to the next slide, please Jeff, and I'll summarise and then we'll go to Q&A.

Slide 34 |Blenrep is well positioned to improve outcomes in RRMM

I think these are the three take-aways. I think the first one of course is this combination of potency, but also manageable eye-related side effects. We could have cited many numbers here on the slide, we have 42%, but we could have also cited various statistics as taken through by Dr Richardson.

I think the second, such as the predicted median OS, I think what we are also now hearing in the market research that Nina took you through, as well as Dr Richardson's own perspective, is that this is a transformational option potentially for patients and physicians, and it can be employed in both the community but also academic environments.

Then the third point is, based on this perspective of DREAMM-7 and DREAMM-8 and the other data, we are going to move into the first-line setting.

Finally, I just want to reinforce the £3 billion peak year sales that we believe that *Blenrep* has the potential to achieve.

With that, Jeff, let's turn it over to questions and answers please.

Q&As

Peter Welford (Jefferies): Hi, hopefully you can hear me. I have a couple of questions. Firstly, just with regards to a comment Professor Richardson made regarding the use of the word 'ophthalmological specialists', I think that's the word he used, hoping to minimise the need for it. I guess to get the GSK point on this as well. When that is mentioned, particularly in the context of the US, are you imagining that you are going to need an ophthalmologist, or do you imagine that you can potentially transition to a world where actually an optometrist is potentially sufficient? I guess I'm thinking particularly of a community setting, the viability of having access to that sort of specialist within the practice.

Secondly, and I guess this is a question on the data. Has there been any work done – I presume this is the case – but is the correlation in DREAMM-7 between those patients that achieved MRD-negativity and survival available. I guess something from a supportive point of view for the first-line as well. I don't imagine there isn't necessarily any reason why it isn't maintained, but any analysis that has been done on that at all.

Then just a quick one for GSK, Luke. Just curious on the peak year sales, potentially you just mentioned. Is that £3 billion-plus still mainly second-line? I guess you're talking increasingly about the first-line opportunity in the way that you want to develop this asset in the future. Are you still regarding that as being underpinned by a second-line use, and any first-line would be largely upside to that peak? Thank you.

Luke Miels: Thanks, Peter. Second-line-plus to your third question, and to correct any first-line would be an upside. Maybe for the first question, Nina, I don't know if you wanted to give colour around our expectations in terms of that framework and potential screening there. Then, if Dr Richardson and Hesham wanted to give some colour to the second question, we'll turn it over to you.

You first, Nina.

Nina Mojas: We can definitely talk about what is going to be the regulatory view about who is going to conduct those examinations. That is a matter of the ongoing conversations we had. We did see in practice ophthalmologists or optometrists, but I think what is probably more relevant is the direction where practising physicians are going to go, and considering that Dr Richardson has a number of years of experience with *Blenrep*, what is his practice may be more credible than our expectation.

Paul Richardson: Thank you, Nina, and thank you, Peter, for an excellent question. I think the ophthalmological aspects of this have been refined very nicely over the last several years because, you're quite right, it has not been an easy construct to have an ophthalmologist evaluate every patient, every cycle. The patients, of course, get concerned about that, and this became particularly in sharp relief during the pandemic, because obviously minimising exposure for patients became very important.

The really good news is that you can have a baseline assessment that may involve an ophthalmological specialist, but thereafter – and we are much more comfortable with the ability to assess patients at the bedside use BCVA as a tool and guide practising oncologists on what we might do. I don't think that in any way diminishes, however, the importance of eye specialist available if things change, but I do want to stress, Peter, that the reversibility is very reassuring, and the construct, the micro-vessel density assessments, have been not correlating with what patients go through. It is very important to understand that, because the grading is quite strict and so ophthalmologists will tell you, 'this patient is clearly much better, their acuity is fantastic but because the micro-cyst density is still there, I have to score this as Grade 3.

What has been very reassuring to us is to understand that and to realise clinically that's not meaningful. We are going to move towards grading that helps clinicians handle that, and basically make the whole construct much less concerning or anxiety-provoking for patients. At the same time, there is this really important construct of how you present this to a patient. If you say to a patient that you are going to have corneal irritation or you are going to have real problems with vision, obviously a patient is going to say 'wait a second, that's just nuts'. That's obviously not the case, and what we do say now to patients is this visual blurring is transient, it's typically non-painful, which is very important for patients to appreciate, and we really refine management such that it is just not an issue.

Then when you juxtapose that, Peter, to some of the real challenges of bispecifics and CAR-T – and I'll give you a real-world example. I said to one of my younger patients, 'how about CAR-T?', and he said 'no, done the homework', he runs his own business, and he said, 'what other options are we going to talk about?' I said we are going to talk about belantamab, and he said 'great', and he is now on the expanded access programme and has been doing very well for about a year and a half.

I think this is a real-world example of a younger patient making this choice because he was less concerned about the ocular toxicity as we put it together for him, and more concerned about some of the downsides and more aggressive approaches.

Nina Mojas: I would just add on this, not trying to minimise, obviously, the importance of monitoring and determining when the patient should be dosed, but this is not the first drug where treating physicians, oncologists, haematologists, had to go through a learning curve on how to use the drug. It's very critical in the beginning because haematologists are not used to evaluating eyesight and eye-related side effects, and it can be very helpful for them to actually seek the support and the help of ophthalmologists. Once they understand what they are dealing with, just like with so many other side effects in oncology that oncologists are used to, or get used to dealing with, we do see the physicians who use *Blenrep*, and then use it repeatedly, are more accustomed to dealing with eye-related side effects. Then it becomes a more natural process to deal with, rather than continuously ask for help from the ophthalmologist.

Paul Richardson: That's an excellent point Nina, and Peter, just to show the obvious example, bortezomib neuropathy, classic, you know we started with real concerns and refined the dosing interval, the same construct actually. It's now a very manageable issue. Carfilzomib and cardiac toxicity, much more serious actually and potentially life threatening, but a similar degree of comfort that we now have. So there are real examples in myeloma specifically, that point to just what you said, Nina.

Hesham Abdullah: Maybe you can help address the second question Peter that you had as well just around MRD negativity and survival, no doubt the correlation that exists between the two and also helping with the adoption of MRD negativity from a regulatory standpoint as a potential target endpoint for early registration in the US. But I can tell you at least to address your question, those analysis are actually ongoing from both DREAMM-7 and DREAMM-8 and stay tuned, they will be presented in 2025.

What I would probably highlight too is that I think as you are probably well aware and Dr Richardson had presented from DREAMM-7, but also we saw the same in DREAMM-8, there's been more than a doubling of MRD negativity rates in both DREAMM-7 and DREAMM-8, now the DREAMM-7 data is statistically significant for MRD negativity, I think that's one important point to highlight. The second is, I think as we start looking at sub groups as well too, whether it be based on response, but also on risk status, I think you have seen the DREAMM-7 data, the DREAMM-8 data in different sub-groups of patients based on PFS, we've seen the drug be very active whether it be in high risk cytogenetics patients, prior not only in LEN exposure but prior LEN refractory patients and low risk sub groups as well too, which I think is also really important to consider.

Shyam Kotadia (Goldman Sachs): Two questions from me please, so the proportion of patients that saw dose delays, on average how long were these delays and what proportion was specifically related to ocular toxicity? The second question, I note that the delays in dosing maintained at least a partial response over time, but could you comment on whether there was a meaningful difference in the overall survival result for those patients that had their doses delayed and modified? Thank you.

Hesham Abdullah: I can certainly help address those as well too Luke and then also certainly refer to Dr Richardson just based on his experience as well too with patients. I will start off first with the second question really around whether or not the dose modifications led to any meaningful differences in outcomes. What we can probably tell you is we have conducted some of these analysis but we will be sharing these at future scientific congresses but what we do see is they have not altered the long-term outcomes of patients, whether it be in terms of response or progression free survival, there is no impact. What's interesting and maybe Dr Richardson you can comment on this as well too, we have seen certainly examples of where patients not only maintain their response but actually the response deepens while they are off the drug, which I think owes to the mechanistic elements that Dr Richardson was referring to earlier with the immunogenic cell death, the duration of response and then how that is maintained over time, even when the patients are in these extended dose interruptions. Dr Richardson?

Paul Richardson: Thanks Hesham, Shyam great question, I would echo everything that Hesham has said and I think in practical terms this is incredibly helpful because dose intervals have not impacted adversely in any way on our response, a response is seen and for that matter the clinical benefits that come with that, be it PFS. In terms of actual OS analysis on this, I am not familiar with that, but I am sure that will be coming from Hesham and the team, so I cannot speak directly to that from the studies, but what I can speak to is my own clinical experience and clearly the patients who have completed therapy from the early phase trials that we were involved in, did very well. We saw real examples of this and I touched on one of my patients earlier who enjoyed three years of PFS benefit after completing therapy on DREAMM-1, which is a very real bonus for a Phase 1 participant and then went on to do very well afterwards. So I think that's just an anecdotal example of what we're alluding to.

Nina Mojas: Can I just add and point maybe to two pieces of data that were published at IMS in September, if I am not mistaken, and happy to share, I think they are on posters. So we looked at both DREAMM-7 and DREAMM-8 at that point and we looked at patients who had 12 or more weeks of interruptions. So one or more interruption of 12 or more weeks and if the outcome of those patients at that point, we looked at PFS, if the outcome of those patient is any different than the overall population and it's actually not, it's exactly the same, so therapy 36.6 months if I am not mistaken, I think they are identical. That is one piece of data.

The other piece of data that was frequently asked, okay but if I need to interrupt my patients very early in the dosing and very early in the treatment journey, we looked at patients who had those interruptions after one or two doses of *Blenrep* and then they had to go to extended dosing. What is their outcome and what is happening to those patients? I believe all except one patient had the same or better response when they stopped, when they continued the treatment. So to Hesham's point, we did look at the data and we actually have quite solid data that indicates that those interruptions are not diminishing the benefit.

Luke Miels: Thanks Nina and I think Dr Richardson referred earlier in terms of the reassurance for patients, particularly at that first relapse.

Graham Parry (Bank of America/Merrill Lynch): Just going back to the monitoring and the requirement for an eye professional for monitoring, I was just wondered the extent to which you've had discussions with regulators and in particular the FDA on this? I just remember the FDA original advisory committee on the original late-line approval was extremely cautious on eye toxicity reversibility, ability to monitor. So although over time perhaps you would hope to get to not requiring an eye professional, do you think you could get an approval without a REMS or do you think a REMS would be needed? What is the likelihood that REMS doesn't require an eye professional examination before you can dose?

Secondly, just the ease of that eye specialist referral, just some of the in the field community position feedback we've had is that actually it's quite hard to get those referrals in place, particularly because the appointment cycles of ophthalmologists differ quite somewhat from the actual dosing regimen of *Blenrep* and it's actually easier for them just to refer a patient into a treatment centre for bispecific CAR-T just talk to the ease of it, thank you.

Luke Miels: Thanks Graham, I think REMS are not unfamiliar of course as you know to multiple myeloma products, maybe Nina and Hesham if you want to provide some colour there and then Nina and Mondher, if you want to just also outline some of the work we are doing on the ground within the countries to put that back office infrastructure and make it easier for physicians to navigate with their patients, that process and of course Dr Richardson if you wanted to add any colour feel free.

Nina Mojas: Let me just start with what Luke mentioned and make it very clear, REMS existence or existence of REMS on its own, is not or should not be perceived as a barrier. Both lenalidomide, pomalidomide, bispecifics,

CAR-Ts, they all have REMS. It's probably likely to expect that we will have some form of REMS the question is what is going to be in that REMS and as you if you look at all these products, REMS on its own is not a barrier to using the drug or success of the product.

Now the question is, what is going to be in that REMS when it comes to ocular examination? In the original discussions in 2020, I think we were in a very different situation. At that point we had a very small number of patients treated, with relatively short follow-up, not fully understanding what is going to happen to patients who did have ocular adverse events. Since then, we have literally thousands of patients now, we know that nobody lost their eye, that all those eye ulcers that we were talking about in the past, are actually not an issue and they are not happening, I think we are now going into the conversations with the regulators from a very different perspective than the first time. What the outcome will be, we can all speculate but, as you can imagine, we are definitely trying to achieve a recommendation that will make it easy or accessible for patients to use the drug.

I think that is a critical factor, particularly for the community setting. We do have – and I think Paul might mention as well – the support of the community physicians in making the drug available, because they are also aware that some element of ocular follow-up potentially could be a barrier.

Hesham Abdullah: I will just build on what Nina highlighted. From our perspective, you heard Nina touch on a little of the differences in terms of the extent of the development programme, and additional data on follow up, reversibility and characterisation of the eye-related side effects. I alluded to this earlier: we have more than 1700 patients treated across the development programme today and, as you have seen from the DREAMM-7 data, we have more than 40 months of follow-up from DREAMM-7 alone, and more than 20 months of follow-up from DREAMM-8. It is a much different position than where we were previously.

You have seen Dr Richardson also go through the data on visual acuity too, and the recovery. I would probably draw your attention to the data that was on that slide and note that more than 90% of patients who experienced a change in visual corrected acuity to 20/50 recovered, and the remainder are in follow-up, recovering. You may ask, are these events monitorable? Absolutely. We want to make sure that physicians are comfortable with how they monitor these patients, and how this collaboration takes place between an eye healthcare professional and the haematologist.

Two, are they manageable? They absolutely are. We know that dose interruptions, and dose reductions, work, but it is important to start at 2.5: we have the data which supports that there is a need to induce the depth of response, especially in these second-line patients, given the tumour burden that exists. Then finally, of course, are they reversible? We have data that says that they are reversible, and to Nina's point, these events don't lead to adverse outcomes in patients with regard to their eyesight. We saw that in less than 2% across both DREAMM-7 and 8 of patients experienced changes in visual acuity to 20/200 and, in those instances, all patients recovered as well, so it is reversible.

It is important to just note that and perhaps I could have Dr Richardson comment.

Paul Richardson: Thanks, Hesham, and thanks Nina – that was great from both of you. Graham, the important point here is that we also have to look now at the survival rate. I am sitting with my patient and I'm saying, you are going to gain basically three years of survival on average. For a patient and a provider, that is enormous. When you think about 'inconvenience', I would really challenge this now, because it is simply the inconvenience of an ophthalmological referral, which pales in comparison to the survival gain that we are talking about. At the same time, this construct that it is inconvenient or difficult is just really – as a specialist, I would say that it is unacceptable for a community physician to say, 'I just can't be bothered to get an ophthalmologist involved, so I'm going to someone to a CAR-T or a bispecific. Frankly, Graham, the gloss is coming off and we are seeing that there are real challenges in real-world practice. For CAR-T, let's be very clear: real-world TRM data right now sits around 10%, and that is treatment-related mortality, but we are not looking at anything like that,

remotely, to the belantamab/mafodotin platforms, where it is less than 1%. I think this is really important to understand in context.

Then you may say, fair enough, the provider has to reach out – but that is the whole other piece which is so exciting. Ophthalmologists, if they can see their patient, and wants to get them quickly and assess them and then hand them over to an algorithm that then moves you through eye care where, if there is an issue going forward, you can then go back to that same specialist – we have found our ophthalmology colleagues have become more comfortable with everything and are becoming much more receptive. They know that it is not a prolonged visit, and they know it is an in-and-out situation. The interactions we have with our ophthalmologists in my own practice has become better and better, and it has become quicker too. It is now provider-to-nurse and, for example, one of my research nurses will liaise with my local ophthalmology consultant, she'll fire me an email off, 'thank you very much', and we'll move on. It has become a much more seamless process.

You might say how does that compare? Let me tell you, if you are looking at a bispecific that goes horribly wrong, with some atypical infection, CNV-reactivation, some atypical organism, a sepsis episode, unfortunately with the older and frailer patients – and I speak directly from my experience with bispecifics – that often result in intensive care, not often, I'd better be careful, it *can* result in intensive care. That is a whole different set of considerations.

Then CAR-T, we move into that space. Miraculous in the majority of patients, sure, but it's a meaningful number, they are a real challenge and I think we all know them. I'm not going to dwell on that, but, Graham, just to simply give you the context now, and I really want to emphasise that. I think the presentation of the survival data changes the discussion dramatically.

Mondher Mahjoubi: If I may add one thing. I'm the Chief Medical Officer and I have the privilege to lead the Medical Affairs teams across the world, and I can tell you, we are more than excited, very, very happy with the opportunity to relaunch *Blenrep* and make it really a successful launch, not just for GSK, but a new medicine that can help transform patients' lives. Medical teams around the globe, and in the US in particular, are not only preparing in terms of resourcing to be competitive, but having a very comprehensive medical education plan, addressing of course the various stakeholders, including patient and healthcare providers about the management of the ocular side effects, but we have also a very ambitious data generation plan.

You have already heard Hesham talking about the expanded access programme, which is already active in a couple of countries, including the US. This is going to be probably the largest ever for GSK, more than 4000 patients are planned to be included, 45 countries will be active. We also have very ambitious Phase 3b/4 studies that will be addressing this proactive dose modification in order to optimise the management of ocular adverse events, and of course, it will cover both academia and community settings as well as various geographies.

Finally, as Hesham alluded to, we are supporting the maximisation of our lifecycle management plan with collaboration in the US and also with major multiple myeloma cooperative groups.

Luke Miels: Thanks, Mondher. Jeff, do we have time for one more question?

Jeff McLaughlin: I think we can take one final question. Thank you, Graham. We will go to Emmanuel Papadakis from Deutsche Bank for the last question. Emmanuel, I'm going to allow you to talk.

Emmanuel Papadakis (Deutsche Bank): Thank you for squeezing me in, sir. Hopefully a couple of quick ones. Apologies if I missed these earlier. Firstly, could you give us an indication of what proportion of second-line patients are actually typically treated in the community setting in the US? Then a couple of questions on DREAMM-10.

Firstly, the timelines for potentially pivotal data, i.e. how soon could we see interim analysis that is potentially registrational on MRD, for example. Then the rationale for the triplet design, given that we have now seen quad studies read out positively such as CEPHEUS in a transplant ineligible setting. I would be interested to hear how relevant you think that triplet sign is going to be a few years down the road. Thank you.

Luke Miels: Thanks, Emmanuel. Nina, correct me if I'm wrong, I think it's around 70% of patients are treated in the community second-line. [*Yes*]

I just want to reinforce that in terms of just the options that Dr Richardson stepped you through in terms of the alternatives in terms of CAR-T not necessarily being accessible to a lot of those patients, and of course, the complexities of a products like teclistamab.

Maybe, Hesham, if you could take us through some of the timelines there in terms of the interim analysis, your thinking as well in terms of quad versus triplet, and of course, Dr Richardson, we would appreciate any perspectives that you have on that choice and logic.

Hesham Abdullah: I would be happy to, Luke, and I'll just start off by highlighting your important question which also highlights the evolving landscape in front-line, acknowledging there are different patient needs and different patient segments and characteristics in newly diagnosed patients as well.

There are patients that may be less fit, that probably couldn't tolerate a quadruple regimen, and there are patients that are more fit that could certainly tolerate the quadruplets as well. What we are trying to do is certainly think about both patient segments. DREAMM-10 is the starting point for development in front-line multiple myeloma. You heard Mondher kindly refer to some of the work that we're going to be doing with certain external partners, cooperative groups and so forth in the academic setting, whether it be in the US, whether it be in Europe, so there will be additional complementary studies that will be coming forward in the front-line setting.

Like I said DREAMM-10 is the starting point with the triplet. You will see some of these other studies look at the quadruplet regimens as well too.

With that in mind, let's get to the question around DREAMM-10, and specifically the fact that the study has of course dual primary endpoints of MRD negativity and PFS. We probably expect the study to initiate imminently, so I would probably say in the next few weeks. That's how quickly it's moving. I would probably anticipate that the first preliminary data readout for MRD negativity would come in the second half of 2027. That is likely to be when we see the first data on MRD negativity from DREAMM-10 with the triplet regimen.

Like I said, stay tuned next year, you will be seeing more in terms of how we think of quadruplets, additional development studies that will be coming forward in front-line multiple myeloma as well. Maybe, Dr Richardson, you can comment these segments of patients in front-line newly diagnosed patients.

Paul Richardson: Thanks so much, Hesham, and Emmanuel, a great question. I think quads obviously have changed the playing field upfront. We have had the results of IMROZ, then followed by CEPHEUS and seen RVd plus isatuximab, we're looking at median progression-free survival estimates that are probably between seven and eight years, if not eight to nine, and CEPHEUS in the same sort of ballpark territory. And that is of course without transplants, and that has transformed the therapeutic landscape in the upfront setting.

I think it's really exciting that bela is moving upfront because there are a number of important reasons for this. Targeting BCMA early I think has already been recognised as an incredibly important construct and something we need to pursue. I very much applaud GSK's strategy. It makes complete sense in the real world to do DREAMM-10, but what is really important to share is obviously the next step is RVd plus bela, and that basically is very, very important because essentially it is key.

In terms of DREAMM-7, there is great confidence built around there with the bela triplet and quads in first-line, and the synergy that may exist this. I think these data also come together to give us a degree of comfort around this strategy being ultimately very successful.

One thing I wanted to close on which I think is really interesting, and again there is a lovely IST that we have launched at Dana Farber, led by my colleague at Mass General, Andy Yee, who worked very close partnership. It's the so-called ISABELA trial. This is actually isatuximab combined with belantamab and pomdex in relapse disease. It has not presented yet, but it's online in terms of it being up and running, but I can share with just briefly that the safety has been excellent. I have actually enrolled four patients in the trial and every single one has responded beautifully, and that's a combination of isatux and bela. It's an intriguing idea because, at this meeting, we've heard about combining bispecifics with CD-38s and the problem has been the challenge of infections and actually added to toxicity.

So far, so good in terms of ISABELA. We've seen nothing like that. It opens an intriguing construct, Emmanuel, that you may actually see CD-38 and BCMA targeting upfront combination strategy going forward with the real synergy being developed.

The final point I would make, there are some patients in whom you clearly want to avoid some of the downsides of CD-38 antibody therapy and that being the case, and especially the infection risk, there is an opportunity to say to a patient 'look, we can tailor our choices to suit you', and bela has a very low infection signal so we would not expect that to be an issue. That actually matters to a very frail person who has significant COPD and for that reason the use of daratumumab may not be so easy, isa may be slightly better. But the fact of the matter is that you can adapt to choose, and with the outcomes we're seeing, I think patients can feel more confident that we are not going to lose ground by so doing.

Luke Miels: Thanks, Emmanuel. Firstly, thank you, Dr Richardson. I trust that everyone found this call useful today. Before we conclude, I just want to acknowledge that the GSK team who, after DREAMM-3, really went back and objectively looked at what lessons there were to be obtained there and built the programme that you are now seeing that enabled us to fully characterise *Blenrep* with the partnership and insight from investigators like Dr Richardson.

I trust that this full discussion today gives you a sense of the perspective and the potential of this product and how excited we are in terms of having an impact on patients with multiple myeloma. We look forward to further updates. Thank you for joining today, I appreciate your interest in *Blenrep* and the company.

[*Ends*]