Getting ahead of respiratory diseases with GSK management
Thursday, 30 November 2023

Introduction | Nick Stone

Slide 1
Hello, everyone. Welcome to our getting ahead of respiratory diseases event with GSK management. As usual, the presentation was emailed to our distribution list earlier today and is available on GSK.com.

Please turn to slide 2.

Slide 2
This is the usual cautionary and forward-looking statement.

Please turn to slide 3.

Slide 3
Today's speakers are our Chief Scientific Officer, Tony Wood, and Chief Commercial Officer, Luke Miels.

And our presentation will last approximately 30 minutes today, followed by 30 minutes for Q&A.

Turning to slide 4, I will now hand the call over to Tony.

Introduction | Dr Tony Wood

Slide 4 | GSK prevents and treats disease in four core therapy areas
Hi everyone, and welcome to our respiratory meet the management event.

As you know, GSK prevents and treats disease in four therapy areas.

Most recently, we spoke to you about HIV.

Today, we'll focus on respiratory, where we have assets across Vaccines, Specialty and General Medicines product areas.

Please turn to the next slide.

Slide 5 | Today's focus

In this deep dive, we'll cover the following areas:

Firstly, our expertise in respiratory disease, where our leadership and innovation have advanced treatment from symptom control to disease stabilisation, with a path towards clinical remission now becoming apparent.

Secondly, I'll briefly cover the role of eosinophils in respiratory disease and the importance of IL-5 in treatment, as shown by our first biologic, *Nucala*, and our ongoing development of depemokimab as a long-acting solution, driving new potential in the respiratory market. Our expectations for depemokimab have increased from £1-2 billion to now more than £3 billion in peak year sales.

Next, I'll turn to the significant unmet need and market potential in refractory chronic cough and camlipixant's differentiation as a best-in-class asset with potential to deliver more than £2.5 billion in peak year sales before finally reviewing key respiratory data readouts from 2024 to 2026 and beyond.

Slide 6 | Leader in respiratory prevention and treatment for decades

GSK has been a leader in the prevention and treatment of respiratory disease for more than five decades.

In asthma and COPD, we started in 1969 with small molecules, primarily to address symptomatic relief through bronchodilation in easy-to-use devices, including most recently with *Trelegy*, our once-daily triple therapy in a single inhaler.

In 2015, we launched *Nucala* for severe asthma, the first monoclonal antibody to target IL-5, which added symptom relief by reducing disease exacerbation. This has led to greater disease stabilisation and reduces the need for oral steroids.

We are also a leader in seasonal respiratory infection, having launched the world's first RSV vaccine. We have a heritage in flu, with ongoing studies using mRNA for high-dose flu and COVID vaccines. While this is not a focus for today, it contributes to our deep understanding of respiratory disease.

Lastly, in addition to reducing exacerbations in severe asthma, we have pursued life-cycle management in other eosinophil-related diseases, specifically EGPA, HES and chronic rhinosinusitis with nasal polyps.

For the future, we're looking at the next wave of innovation, including long-acting options and further evaluation of the role of eosinophils in asthma in pursuit of clinical remission and, ultimately, disease modification.

Slide 7 | Delivering competitive growth at scale

Together, our respiratory medicines and vaccines are driving competitive sales growth, delivering over £11 billion in 2022 with *Trelegy* and *Nucala* as major contributors.

Trelegy is the most prescribed single inhaled triple therapy worldwide and is on track to deliver over £2 billion in 2023.

Nucala has already contributed over £1 billion in sales this year, and continues to grow in a market with low virologic penetration. We'll talk more on this later.

Slide 8 | To treat respiratory disease remains an area of high unmet need

Even with these major advances, respiratory disease remains an area of high unmet need and significant burden for patients and health systems.

In particular today, we'll talk about the role of eosinophils in asthma, COPD and chronic rhinosinusitis, and the unmet need in refractory chronic cough.

Low T2 disease, which will I will explain later, also remains poorly addressed and this will be one area of BD focus for us.

Slide 9 | Advancing treatment goals to clinical remission

For over five decades, our ambition in respiratory has been to prevent and treat disease by reducing signs and symptoms, addressing treatment resistance and slowing disease progression.

We have addressed symptom relief with bronchodilation, reduced exacerbations with a first-in-class biologic targeting IL-5 and are now on a path towards clinical remission. This means helping patients who suffer from asthma achieve four things; to be exacerbation and OCS-free and to live with symptom control and stabilised lung function.

Ultimately our goal is to change the course of disease, slowing it down, stopping progression and even reversing previous damage.

Let's hear more about this from a patient's perspective.

Slide 10 | Aspiring to achieve clinical remission in specific types of severe asthma

Video with Shelby and Joelle:

I had never heard of clinical remission until about two months ago but I do believe that clinical remission is possible in severe eosinophilic asthma.

If I could speak to a younger version of myself I think I would just say not to lose hope. There is definitely a moment when I was trying medication after medication and it just wasn't helping and I didn't want to go on any more medications because it was just a letdown each time, so I would say not to lose hope.

My hope of all hopes is that she would eventually achieve clinical remission.

[*End of video*]

Thank you. Turning now to the biology of IL-5.

Understanding the biological effects of IL-5 | Dr Tony Wood

Slide 11 | Understanding the biological effects of IL-5

Understanding IL-5 biology is important to achieve even more for patients and a better appreciation of its role will create more opportunity, so let's step back and talk about this biology and its importance in treating eosinophilic disease.

Slide 12 | Eosinophils and IL-5 play a central role in controlling inflammation and its healthy resolution

In our development of *Nucala*, we've shown that T2 inflammation is a key driver of exacerbations in severe asthma. What do I mean by T2 inflammation? This is how the immune system reacts to pathogens and antigens. It's especially important in the lung where a large surface area allows massive exposure.

A key immune cell in T2 inflammation is the eosinophil and IL-5 is a powerful pro-inflammatory cytokine that is responsible for the maturation, proliferation, activation and migration of eosinophils. Importantly, IL-5 is also involved in the healthy resolution of inflammation, including the programming of wound healing versus fibrosis.

With *Nucala*, we have shown the clinical effects of modulation of the T2 inflammatory response, deepening our understanding of the role of eosinophils and laying a foundation to better understand the science of disease modification.

Slide 13 | Nucala sustained clinical remission in real-world evidence studies

Our leading work on clinical remission with *Nucala* creates unique insights for the next phase of innovation and indeed our BD focus. In a post-hoc analysis of our REALITI-A study, *Nucala* demonstrated that 37% of patients with severe asthma achieved all four components of clinical remission. Let me remind you of those again: that is exacerbation and OCS free, symptom control and stabilised lung function which was sustained for over two years.

Following this, we have a comprehensive evidence-generation programme to further examine clinical remission and explore T2 biology at the interface of healthy wound healing and fibrosis.

Slide 14 | Leading the science in COPD with an eosinophilic phenotype

As part of the life cycle management, we are also continuing to evaluate eosinophilia in COPD. Our previous phase III trials, METREX and METREO, were the first to attempt the demonstration of efficacy with a biologic in COPD showing a reduction of 24% in moderate and severe exacerbations in patients with high blood eosinophils of ≥300 cells/ μL.

As you are aware, only one of these studies demonstrated statistical significance and we received a Complete Response Letter for the application. To address this we initiated a third trial taking into account FDA feedback.

Our MATINEE phase III trial focuses on patients with higher eosinophil counts which have been associated with higher exacerbation rates and poorer outcomes. It is also a purer COPD population and includes patients with emphysema. Seeking to confirm the efficacy of *Nucala* in COPD, MATINEE is expected to read out at the end of next year.

A positive outcome will inform our approach for further life cycle management for depemokimab in COPD, a potential best in class next generation IL-5 treatment for eosinophilic-led disease.

Let's talk about that next.

Depemokimab | Dr Tony Wood

Slide 15 | Depemokimab
The next slide, please.

Slide 16 | Depemokimab: next generation IL-5 enabling twice-yearly dosing
Building on insights from *Nucala*, we are developing depemokimab with more potent pharmacology, a longer half-life and, ultimately, an improved twice-yearly dosing schedule. In phase I in the higher doses tested, we saw a sustained reduction of eosinophils for six months following depe treatment.

Backed by extensive PK/PD modelling, we progressed straight to phase III in four indications: asthma; chronic rhinosinusitis with nasal polyps; eosinophilic granulomatosis and with polyangiitis; and hyper-eosinophilic syndrome.

We expect depemokimab to demonstrate efficacy benefits due to improved adherence from twice-yearly dosing, and our clinical plan will review outcomes associated with remission. We'll build on this with a comprehensive real-world evidence programme starting at launch.

This is just one example of smart risk-taking in R&D, using our knowledge from *Nucala* and accelerating development of a next-generation biologic in two versus seven years.

We'll have our first readout in asthma with SWIFT-1 and SWIFT-2 in the first half of 2024.

With that, let me hand over to Luke

Depemokimab | Luke Miels

Slide 17 | High economic burden and a clear unmet medical need

Thanks, Tony.

The core assumption that we have when we look at how this market's likely to evolve in asthma and COPD is that we're going to see a high usage of biologics, and as you can see on the chart here - asthma on the left and COPD on the right — this is going to drive a material level of growth, and it's our central hypothesis that depemokimab is going to be a key component of that adoption.

Slide 18 | Depemokimab: improved real-world efficacy with improved dosing

If we look at what are the components of depemokimab that are likely to drive that change in practice, it is intriguing right now, and this reminds me of mid-'90s, when you looked at TNFs and other biologics, we're in the early stages of an adoption of biologics within asthma, and of course more recently, nasal polyps, interestingly with ENTs seem to pick this up quite quickly, in contrast to where we are today with biologics in rheumatoid arthritis, so I think it's fair to say that we will ultimately see this level of penetration over time, particularly as you see physicians, HCPs in training, adopting biologics and having that experience right from the start of their clinical practice in pulmonology and allergy in particular.

If you look specifically at the profile of depemokimab — and of course we have tested this intensively, we'll go through this shortly — in a nutshell and why we think this is going to shift practice, the first one

is lower frequency of shots, you're going to have better compliance, and so that's likely, we know consistently, across multiple targets and multiple settings, this is likely to translate into better efficacy.

The other interesting element, as Tony mentioned earlier, this concept of clinical remission, and embedding that in our studies, and this is something that could be very attractive to physicians in the medium term.

Then ultimately when we look at the other elements, specifically at patient level, real world practice, we look at artificial things which are clinical trials, when we look at *Nucala* in the real world, and this is consistent with longer-acting drugs - and we've seen this in psoriasis and of course people on the call are very familiar with those analogues – these do materially improve the experience of patients, and ultimately the efficacy. It's interesting, when we look at *Nucala*, and it's true for other biologics in asthma, if you go 12 months out, typically you lose six out of ten patients at that point, and that's a complex component but a big part of that is the burden on the patient from multiple shots and physician visits.

Again, to go down from 12 shots to two per year, for example, the complexity around co-pays, the Part B versus Part D element, just the logistics, the physician's offices to administer this and navigate reimbursement pathways, these are all elements which simplify the experience for the patient and the physician and should drive a better outcome in terms of efficacy.

Next slide, please.

Slide 19 | Focused development to drive breadth of indications in two years
Now, the other element here is not only are we going to see broader penetration and expansion of use through a simpler offering, which depemokimab is, when you look at the life cycle programme for *Nucala*, it's taken about eight years from the initial indication to get through to this set of indications you can see here, with nasal polyps being the most recent.

In contrast, with depemokimab, because the targets have been de-risked, and we've just taken a more proactive approach to lifecycle management, it's going to take about two years from the initial indication in severe eosinophilic asthma right through to HES now. Obviously then we'll have COPD, which is de-risked hopefully with *Nucala* and what we've learned with the Sanofi programme, so it's going to compress this uptake, and so physicians will be able to use this in a broader number of patients, in a broader number of settings, and will also be able to interact around the label with different

physician groups who could influence the usage of this product.   And it is a very broad offering, as you can see, in contrast to the alternatives for physicians in the right-hand side of the slide.

Slide 20 | Depemokimab: high HCP willingness to prescribe, strong patient preference

This is reflected in the market research. Obviously, you can imagine that we do a lot of work around the target medicine profile and what we expect that we'll realise through the clinical programme. I think this first line for me was really compelling. We asked 200 physicians, on a score of one to seven, how do you score the profile of depemokimab in severe eosinophilic asthma, with one being no difference, and six and seven being defined as highly beneficial.

You can see there that 73% of physicians picked either a six or a seven score, which is, again, very compelling and you don't typically see this level of favourability for a product at this point.

Then when we looked in different market research around where would you use this product, in what type of patients would you employ depemokimab, it is interesting that you see here that 57% said they would look at bio-naïve patients, which I think makes sense on many levels, which I will get into shortly. But intriguingly, and I also think encouragingly, 66% of them said they would also consider switching current patients to depemokimab. These two things are not mutually exclusive: you have an existing bolus of patients who, as I said, we are losing a lot of these patients after six months up to 12 months, but they could be ripe for re-challenging with a simpler, more effective agent.

Then, when you ask the patients themselves, you can see here that six out of ten say that a six-month injection would be attractive. I think that is relatively commonsense: I think most people would rather have two injections a year, rather than 12 or six. Then, when you look at how they would behave if their HCP recommended it, you can see that 87% indicated that they would be open to that. That becomes important, because there is a material number of patients who are resistant to biologics because of fear of needles: this is not an inconsequential number — it is about one in five, depending on the data you look at. With this, again, when you aggregate all of these elements, you start to see an attractive product.

Slide 21 | Depemokimab share will come from all biologics

One of the questions we are often asked, when meeting with investors is, will this just ablate *Nucala*? It brings back memories because, when we were launching *Trelegy*, we had a lot of similar questions — are you just going to cannibalise your own business? What we have shown in the same target

population of physicians is that that is not the case. It is more than 60% of our business on *Trelegy* that is coming from non-GSK products. I think we can replicate this here with depemokimab. In many ways, we are actually more confident about that, and the stats here tell the truth. If you look at it, about 50% of the business will come from IL-5s – either *Nucala* or *Fasenra.*

When we look at the usage of Fasenra, the main driver – at least in the stats that we collect, from the market research that we collect – is frequency of administration. This population is ripe for targeting, either those on Fasenra or physicians who favour Fasenra because of the frequency of administration. Interestingly, it is really only about a quarter of these patients that physicians would imagine are either not using *Nucala* and replacing with depemokimab, or shifting patients off *Nucala* and employing depemokimab in its place.

You can see there the TSLPs, Dupilumab, Xolair – they are also ripe for targeting in this area and represent a sizeable proportion of patients. Also, what I think is exciting here is that you have a sizeable population which is naïve and has not been treated before, and you can also see that 20%, as I was mentioning earlier, that are largely driven by fear of injection.

I think these are encouraging numbers. We obviously have to achieve this profile in the clinical programme. It is compelling.

Slide 22 | Depemokimab: increased sales potential from £1-2 billion

Pulling all this together, you have a product which is simpler to use, offers the potential in the real world of demonstrating sustained efficacy, with simpler ways of administration, simpler ways of navigating reimbursement. There is a lower burden for commercial patients and Medicare patients in terms of reimbursement and copays.

When you build this picture up and look at the interplay between *Nucala* and depemokimab - this is our estimate; of course, it is a forecast of what the pattern would be. In 2022, once depemokimab is introduced, we would see some erosion, as the market research earlier would indicate, but we expect that actually to be offset by the successful implementation of a *Nucala* COPD label as we enter a new subset of patients, and if you remember the first line represented, there appears to be a high level of interest and that's certainly been what we have seen in some of the analysts' notes around the news that Sanofi has signalled over the last couple of days.

And then you look at depemokimab which is really driving the bulk of this uptake in severe asthma and then the life cycle, so EGPA, HES, nasal polyps and then COPD are incremental above that, but we expect the bulk of this business to be driven by that classic eosinophic asthma, severe asthma patient, where there is still a very high unmet need, and about half these patients still aren't adequately controlled on their current treatment. That's the full picture there, and if we aggregate all of that, you are looking at about £3 billion or more than £3 billion in revenue for depemokimab at peak and when you also include *Nucala* there with this relatively stable base business of *Nucala*, then that figure is above £4bn.

Slide 23 | Camlipixant

Now before we go in depth into the clinical and commercial arguments for camlipixant, I think it's appropriate that we give you a perspective from the patient, so you will hear from Sherisse who is suffering from refractory chronic cough, so we will just now go to the video and then after that I'll come back and we will get into some more depth with Tony into this programme.

Slide 24 | Refractory chronic cough patients often experience an emotionally taxing and lengthy journey as they seek to resolve their cough

Video of Sherisse

A chronic cough trigger can last for me, it happens like this, like in spurts, but the spurts can last up to like at times like six minutes, depending on what caused it and also depending on if I'm not near water.

So imagine I'm teaching and I keep running into these five to six-minute cough spurts and having to pause my classroom while I go handle a chronic cough. Eventually they had me just doing admin work in the office, so as of current I am fully disabled because I am unable to do what it is that I am experienced and trained to do.

[*End of video*]

Thank you to Sherisse.

Slide 25 | Refractory chronic cough is a distinct neuropathic disorder

Hopefully that was illuminating for you and gives you more of a practical demonstration of what the burden is like for a patient suffering from refractory chronic cough. If you look at the numbers, when we

did do the BELLUS deal a number of investors contacted us and said 'How big is this population? I don't hear people coughing around me every day, what's the epi here?'.

You can see on the top left-hand side if you just look at people who have been coughing for more than eight weeks, in the larger countries you can see a population of 28 million. That's not a population that we use in our models. We then take a more strict slice where you look at individuals who have been diagnosed with symptoms for more than one year, and you can still see that's a very material number of ten million people.

When you look at the profile and the burden that these patients have, so typically two-thirds of them are females and 50 to 65 years of age, and you can see 500 coughs a day. Obviously some people are a lot higher than that, some people are lower than that.

Urinary incontinence is very typical, so the social consequences of that, of not only coughing but the psychological downstream effects of that and depression, you can see here is in about half those patients because of the anxiety, the impact on their partner and the insomnia, and also just the social isolation that comes with coughing, particularly fits of coughing, and of course in more extreme situations, you can see some of the elements below on this slide in terms of vomiting and fainting. So it is a disease with a lot of burden and if we go to the next slide.

Slide 26 | Patients have few effective treatments; no licensed targeted therapies*

If we look at the treatment pathway that these patients typically have to navigate, and this may be partly because there are no licensed therapies available, but typically it is a disease of exclusion.

When someone presents with a chronic cough, more than eight weeks, the first reflex of the physician of course, very sensibly, is to try and remove or exclude more serious diseases such as lung cancer, asthma, bronchitis, COPD, IPF, reflux of course is very common as a reason for cough, and ultimately if they get there or there's no underlying disorder that's identifiable then they are classified as having refractory chronic cough.

The challenge here, if you look at the bottom right hand side of the slide, typically these patients have to navigate three or more specialists in 50% of the cases, sometimes it's more than that, and even if they are diagnosed with refractory chronic cough they tend to rotate different options, because the therapies here, you can see three or more therapies.

So, difficult to get a diagnosis and frustrating to get an outcome that is satisfactory for that patient.

Slide 27 | Refractory chronic cough: high burden, low treatment satisfaction

If we go to the next slide, this is direct surveys of physicians, so, is this a serious disease – again, going back to the original question that I mentioned at the start of this section, is this an sizable disease, is it a real disease with material burdens that would encourage treatment – and you can see, 91% of physicians managing refractory chronic cough say it's extremely burdensome.

Then if you ask them, what are the options that you have for treating these patients, you can see 3% are satisfied with the options, so 97% say they're very unsatisfied.

Then when you ask them, okay, assuming the drug is well-tolerated and there is a new treatment approach, would you employ it in these patients, even if you were not deeply and fully familiar with it? You can see over three-quarters of pulmonologists and allergists who treat the bulk of these patients would say yes, I agree or strongly agree, in terms of trying a therapy.

You have a high unmet need, you have a sizeable population, you have physicians who are frustrated with the options available, so it is ideally primed for an effective and well-tolerated treatment.

With that, I will hand over to Tony.

Camlipixant | Dr Tony Wood

Slide 28 | Camlipixant: potential best-in-disease medicine for RCC

Let me now describe the biology of Camlipixant.

P2X3 is a validated biological target implicated in cough reflex hypersensitisation.

We know that the activation of P2X3 receptors increases the excitability of airway sensory nerve fibres, contributing to excessive cough. Inhibition of P2X3 receptors, therefore, could normalise the overactive cough reflex and reduce cough frequency.

In this medicine class, we also know that selectivity for the P2X2/3 receptor has proven difficult, with a consequence of taste disturbance given the presence of P2X2 on sensory taste nerves.

Camlipixant's high selectivity for P2X3, therefore, provides potential efficacy and tolerability benefits. Camlipixant is 1,000-fold more selective than its current competitor, so has the potential to be a best-in-disease medicine for RCC.

In order to assess the true potential of camlipixant, a placebo-adjusted reduction in cough frequency is used. As illustrated here, camlipixant demonstrated a clinically relevant reduction in cough frequency at all doses tested in the phase IIb SOOTHE trial.

Importantly, across all doses, there were low rates of taste-related adverse events (≤6.5%), and zero discontinuations related to taste.

Slide 29 | Camlipixant: Phase III CALM programme, data expected in H2 2025

Looking ahead, data from our phase III CALM programme for the 25mg and 50mg doses is expected in the second half of 2025.

Following the FDA's Advisory Committee on gefapixant on 17 November, committee members acknowledged the significant unmet medical need in RCC, but suggested that a more robust difference from placebo and the removal of potential confounding by taste effect would have been more compelling. They also suggested looking at different endpoints that better reflect the patient experience.

These evidence requirements identified by the committee are well considered in our programme for camlipixant. In fact, the camlipixant phase III design was optimised post-deal close to ensure we capture the true efficacy of the molecule. The optimisation was done in close collaboration with the FDA and includes a number of key elements.

First, prior to dosing, all patients recruited into the CALM programme must be adjudicated by an independent panel. This panel look closely at the patient's medical history, to confirm a diagnosis of refractory chronic cough.

Second, the dosing phase of the trial includes a placebo run-in period, prior to randomisation in treatment groups. We know that cough trials typically experience a placebo effect, and by including this placebo run-in phase, we will reduce both baseline variability and an anticipated placebo effect.

Third, we are enriching the trial with patients with a higher cough frequency.

Finally, the high selectivity of the asset is expected to reduce off-target effects, like dysgeusia, which could lead to unblinding.

With these points in mind, we are confident that the phase III programme can assess the true potential of camlipixant.

With that, I will hand back to Luke to wrap up the presentation.

Camlipixant | Luke Miels

Thanks, Tony.

Slide 30 | Camlipixant: strong physician preference versus competition

What is always compelling and engaging when we look at an asset is that you have a viable hypothesis, that the underlying mechanisms makes sense for physicians as to why they would see firstly efficacy and then, secondly, why would there be a differentiation between our molecule and a potential option available to physicians within the same class.

This is market research that we have done based on the profile of gefapixant, and also with real-world experience of physicians using gefapixant in Japan. You can see here that taste disturbance is a problem, and so we spent a great deal of time looking at the data during the due diligence with BELLUS to really understand. Mechanistically, we have a high confidence of seeing a difference here between gefapixant and camlipixant, and that then presents itself when you look at the HCP preference. You can see here that 73% believe that camlipixant is the best-in-class molecule. You can see, again, that 85% prefer it because of the taste disturbance. So, even with neutral efficacy, they prefer camlipixant because of the lower consequences around off-target taste disruption. For me, this is very exciting.

Slide 31 | Respiratory medicines growth drivers

If we go to the last couple of slides, when you look at this, for the consequence structurally, strategically to the business, again, we think we can keep *Nucala* growing, and that it is a very durable business and it has a position. But the bulk of practice will shift to these longer-acting products like depemokimab, and I mentioned the analogues that we have had before, in a number of very similar settings, where longer-acting treatments have really shifted practice. We have seen more people treated, staying on

longer, and physicians electing to use these products ahead of the shorter-acting products. We are very confident that will occur with depemokimab.

Again, with camlipixant, a high number of patients, high unmet need, and a compelling profile of a product which is attractive to physicians and should help patients.

Slide 32 | Forthcoming catalysts

If we move to the last slide before the Q&A, if we look at the forthcoming catalysts, of course COPD, the read-out there, as Tony covered earlier, we have a high level of confidence in this space, based on the insights we got from our own programme and the recent success that Sanofi has had has further increased that confidence.

With depemokimab, SWIFT 1 and 2 are on track for a read-out in the first half of next year, and then we have nasal polyps.

NIMBLE is the switch study, where we have taken people on *Fasenra* and *Nucala*, and switching them across to depemokimab. This is an important study for us. And then we have the other lifecycle programmes that I mentioned, to get this two-year timeframe post-launch for depemokimab. And then CALM 1 and CALM 2, for camlipixant, reading out in 2025.

Again, to reinforce, as Tony has covered and I have also mentioned, we have taken insights from our discussions with the regulator and the public information that is available on Merck which have enabled these programmes to be designed to give us confidence that they are going to read out as we expect for the target medicine profile.

With that, I will go to questions with Tony.

Q&A

Nick Stone: Thanks, Luke and Tony. Obviously that was a great overview of Respiratory, particularly the significant opportunities that we have ahead of us for both depemokimab and camlipixant.

Given where we are in terms of time, we will now start the Q&A, but we will aim to finish by about two o'clock, obviously depending on demand and we will see where we get to. As a reminder, to ask the

question in Zoom, please raise your hand using the icon in the menu bar: I will then open your line so that we can have you ask your question. If you have joined Zoom using the telephone, please press *9 to register a question, and *6 to unmute if needed.

Could I also remind everyone to limit questions, at least in the first instance, to one or two, just to be fair to all participants.

With that, we will take our first question from Simon Baker. Over to you please, Simon.

Simon Baker (Redburn):   Thank you, Nick. Thank you for the presentation. I have two questions if I may. Firstly, on depemokimab, in re-engineering the antibody, you increased the affinity by about 30-fold and slowed the curves about two-fold. I was just wondering, how generalised is that approach to other antibodies? I was looking – and you have not disclosed much of what you did for probably understandable reasons. And specifically on depe – what do you think is the real driver for the six-monthly dosing. It is the higher affinity or the lower clearance?

And then on to a more general question on eosinophilic asthma, could you give us an idea of current testing rates by severity to determine that eosinophils aren't the driver of asthma in mild, moderate and severe? Thanks very much.

Tony Wood: Hi Simon. Why don't I get started on Simon's question with regards to depemokimab and extension of the pharmacodynamic effect? Simon, there is nothing special about this that would mean it's solely applicable to depemokimab. It's fairly straightforward. In depemokimab's case, of course, we had confidence in measuring the efficacy of the molecule because of what we have learned in a translational sense from assays from *Nucala*, but in general the reason why you see the extended dosing frequency is a combination of intrinsic half-life and also the ability to, let's say, overdose because of the increased potency giving us a longer pharmacodynamic effect as well.

Both make a contribution that is entirely calculable on the basis of the PK/PD models that we have, and we are able, of course, to go to that higher dose in the first instance because we are so confident with the safety of the mechanism, so generally applicable, and following very, what I would call, standard but sophisticated modelling behind it in terms of our approach to confidence in translation.

Luke Miels: Yes, and Simon, the bulk of patients that are being managed by pulmonologists, so those at the severe end of the spectrum are tested. As you know, it's a relatively simple blood test and the

guidelines are very clear on that factor. They also encourage multiple testing because we know, and we've used this insight in our COPD programme, that these levels can move over time. If you look at the background epi, it's around 85% of severe patients are eosinophilic, their disease is eosinophilic in nature, so it's very rational to test for that.

For the milder patients, the penetration is less, as you would expect, but it's something that we have actually been trying to shift in the US with promotion to *Nucala* in high user primary care doctors and have had some success on that front.

Nick Stone: Thanks, both. If we take our next question from Richard Parkes at BNP Paribas.

Richard Parkes (BNP Paribas): Thanks, Nick. Hopefully you can hear me okay. Yes, I will stick to the two questions. Firstly, can you talk about what percentage of COPD patients are likely to be eligible for biologics treatment based on entry criteria to MATINEE and how that compares to the Dupixent studies and just clarify the differences in recruitment criteria between MATINEE and the previous studies. Is it just eosinophil cutoff or any other differences?

And then secondly, one of the Advisory Committee concerns over gefapixant was not just the dysgeusia but maybe that that high discontinuation rate really reflects what benefit patients were experiencing was modest and maybe just reflecting an imperceptible change in cough frequency.

How confident are you that you will ultimately have a profile where you will have a more meaningful clinical benefit in addition to less incidence of dysgeusia? Thank you.

Tony Wood: Let me take that, and Luke might want to comment on the general population considerations in COPD. I'll make a couple of points in answering your question, Richard. Let's talk first of all about the difference in patient populations between the Dupi studies, BOREAS and NOTUS and our ongoing studies.

The important difference to stress is we have included a broader COPD population that includes emphysemic patients, about 30% of the COPD population. What we have also done in response in the MATINEE design was in response to the CRL, so as well as higher EOS as you have indicated, we have also been careful to recruit a purer COPD population.

If you look at the impact of both of those things and what that might do in terms of relative reduction in exacerbation rates compared to the Dupi studies, you can find a sort of indicator of that in some of our published phase II data that shows that when we look at a more bronchitic population, which is the one that Dupi addressed. Those individuals have more reactive and responsive airways, and with that in mind we achieved in our phase II studies looking at that selected population efficacy in terms of exacerbation reduction which is very much in line with the sort of results that you're now seeing reported out for Dupi.

What I'd also emphasise, of course, is that we also have extensive patient safety for the use of IL-5 in that population as well. We're out at now more than 100 weeks, and we don't have the hyper-eosinophilia observation that comes with Dupi.

I'm confident in terms of our design, addressing a broader population and achieving efficacy, and continuing to underscore the role of the eosinophilia in COPD, which is something that's important to stress when we look at the latest data for Dupi – that, if anything, just increases my confidence that eosinophilia as an approach in COPD is important.

I'll pause there and let Luke add what he wants to in COPD before we go on and talk about the magnitude of clinical benefit in the CALM studies.

Luke Miels: The only thing I would add is peak patient population at the time of expiry is over 100,000 and it's under 250,000, because of emphysema, the EOS cut-off, etc., so it's a specific population, but that's the number range issue you should model for COPD.

Tony Wood: Yes, Richard, and then in terms of magnitude of clinical effect and what's deemed as significant relative to placebo in refractory chronic cough, there are a couple of features that I just want to re-emphasise in terms of our design that I think play into the reality of efficacy.

First of all, let me go back to the three features that I mentioned earlier in the presentation. It's important to recognise that cough is quite a heterogeneous disease and therefore our focus to an independent committee adjudicating the entry of individuals as presenting with refractory chronic cough is important. The placebo run-in that looks at the trajectory of baseline effects is also important; and then lastly, as I mentioned, we've recruited into CALM 1 and CALM 2 in a way in which we're enriching for those individuals for which we think the mechanism is likely to have the greatest therapeutic effect.

With all of that together, and then I'd just direct you back to the efficacy that we saw in the phase II SOOTHE study, which is indicative of a higher reduction in chronic cough frequency than is the case in the general population. This is a matter of a better study design, a better molecule, and ultimately that allowing us to target it at a likely more responsive patient population who will see greater clinical effect.

Nick Stone: Thanks Tony. If we take our next question from Andrew Baum at Citi.

Andrew Baum (Citi): A question for Luke in relation to depemokimab: given the method of administration, it's obviously going to be done by the clinician, can you just remind us for *Nucala* and the incumbent competitors what percentage is self-administered versus physician-administered; and given this will require a buy-and-bill dynamic with the clinicians, how problematic is that in transitioning patients from one to the other?

Luke Miels: Andrew, for self-administration, Dupi is 100%, which is, I guess, expected. *Fasenra*, based on our figures is about 80% self-administered; *Nucala* is 73% on the latest numbers we have; and then *Tezspire* is 55%, but of course the self-admin, from memory, I think only came in in February.

In terms of moving patients back and forth, that certainly influences some of the assumptions that we make, naïve versus switch patients. If you look at the total insurance spread linked to that, we think it will peak at about a third of these patients, just over a third of these patients are going to be commercial, so that Part B/Part D dynamic is important.

I think the bulk of the business for this product ultimately will come from Part B, and we have some thoughts there around access and making that very compelling for the physician and the patients as well.

Nick Stone: Thanks, Luke. The next question will come from Jefferies and, in particular, Peter Welford. Over to you, please, Peter.

Peter Welford (Jefferies): I have two questions, firstly on *Nucala*. I am curious, when you look at the graph you showed of the peak sales potential – I guess, given everything you have said, is the £0.5 to £1 billion peak in COPD, which is un-risk adjusted, is that conservatism on your part, or is it something we should bear in mind when we consider why, given the size of the population you have just talked about, you see that as an eligible COPD peak sales for the drug?

I guess, related to that, what have you assumed for *Nucala*, to do with potential either biosimilars or, I guess, possible IRA impact?

Then secondly, on camlipixant, just on the phase III, this is to do with the trial design. Firstly, the unexplained chronic cough element – I think another thing that was introduced by the FDA, the Advisory Committee, was whether or not potentially, by including unexplained cough, you are potentially hiding an undiagnosed condition. Could the study potentially be analysed in the separate populations respectively, so refractory versus unexplained, or any thoughts as you could potentially satisfy FDA's concerns on that issue.

Luke Miels: Peter, based on our intelligence, there are two biosimilars in the clinic, very early stages in China. I think there is one in pre-clinical outside of China, so with our modelling, we would not expect to see a biosimilar before 2031. There will be some IRA effects that we have modelled in that number. The numbers we give you are always at the mid-point, so by definition, conservative.

In terms of COPD, yes, it's interesting. When you look at the IL-5 class, it's a bit of a coin toss when it comes to physicians' favourability between *Fasenra* and *Nucala*. About a quarter of the HCPs love *Nucala* and use it extensively and don't use *Fasenra*, and about a quarter of the doctors use *Fasenra* and don't use *Nucala* as much, but the other 50% are agnostic. They like the mechanism, they use both products, so you don't have this embedded group. That's why, when you look at the market research there, it lines up with it, 25% of the business will come from *Nucala*.

Because *Nucala* is obviously going to launch in COPD earlier, we think we will pick up those patients. There is a segment of patients that physicians don't want to move, and there are also patients who say 'look, I'm stable, don't move me', but the other thing is, as I mentioned earlier, it's a lot more dynamic than we think, and we lose six out of ten patients at 12 months. These patients are moving back and forth between options, or out of the biologic class and back into the biologics class.

In terms of depemokimab and IRA impact, we have a pretty clear sense that payers will see this as differentiated, and following the core clinical programme, our intention is to be very aggressive with the real world evidence programme. We have some great data from *Nucala*, more coming up. It clearly shows, as you would expect, a correlation with adherence and efficacy, and we also know that lower shots lead to higher adherence, so if you connect those components up, we should see better results in the real world and working with payers in the US.

Tony Wood: Peter, yes, it was an interesting comment, I thought, because there are two ways to look at 'unexplained'. The first one is an individual who has not gone through a full diagnosis cascade to identify underlying pathology. As you can see from our clinical study design, there is an independent adjudication committee that is addressing that particular issue with regards to entrance for the CALM 1 and CALM 2 studies.

For those who have been triaged and for which there is no then determined underlying effect, I think you're in the simple position of then reflecting that camlipixant is the best opportunity they have ahead of them to reduce remaining cough. Indeed, one might look at this as the emergence of a cough class that we might call a neuropathic cough in which the origins of the enhanced coughing frequency are associated with a change in the distribution of receptors in the upper respiratory tract, so in terms of that aspect of 'unexplained' which we can deal with, it's accounted for in the phase III design. In terms of that which remains of 'unknown origin', showing that we can reduce coughing frequency in that class with an agent that is addressing a particular aspect of potential neuropathic pain I would argue is an appropriate approach for those folks.

Nick Stone: Thanks, Tony. Just before we go to our next question, just as a brief reminder, if you need to ask a question on Zoom please raise your hand using the icon in the menu bar and obviously we will then open your line. If you are on the telephone, please use star nine to register for a question and you may need to use start six to unmute.

Our next question will come from Seamus Fernandez at Guggenheim, so over to you please, Seamus.

Seamus Fernandez (Guggenheim): Hi, thanks for the question. I just wanted to go through the opportunity in chronic cough more from an access and payer perspective and how you are thinking about the pricing that would be realistic in the market. I know you are unlikely to talk about price, but maybe just help us understand if you see this as a product that would fall above the specialty tier in terms of pricing or below that relative to the Medicare pricing dynamics.

And then also uptake in new areas like this tends to be quite slow from an access perspective. Just hoping to get a better understanding of how you see the launch of this product evolving over time. I see the opportunity from an upside perspective, but the pace of uptake I think is something that everybody would like to try and understand a little bit better. Thank you.

Luke Miels: Thanks, Seamus. The typical patient, about three quarters of them are commercial patients so in our models we had a lot of insight for this obviously from *Nucala* and *Trelegy*, so we assume classical abandonment rates of about a quarter to a third of patients at that point, and I will get to the pricing range in a second.

Adherence you should model more than 70% based on the market research because this lines up with classical high morbidity diseases, and there are lots of analogues that we use there, ranging from rheumatoid arthritis, complicated diabetes, etc., so yes, you have those commercial patients and we can assist them with copays.

Now in terms of the pricing range, we are very deliberately pricing below that threshold, so the price is somewhere between 600 and 800 in our models. Our market research has done a lot of that with payers. We have spoken to over 45 payers, probably more than that now, and it indicates that they are very receptive to the introduction of this because of course the unmet need is very high.

In terms of the adoption, all the market research from pulmonologists and allergists, and these are the primary drivers for refractory chronic cough, are very clear that they will adopt it and adopt it quickly. We know these individuals very well from our existing business.

The other intriguing thing is we have looked at analogues like triptans with migraine where you have unmet need, pretty non-existent standard of care and you see very rapid uptake, so acceptable price range, established population.

The other thing, when you look at the patient populations, we are really looking at the cohort of people who have been coughing for more than one year and who are being managed by specialists, so that is under two million in the US and similar numbers in Europe. When you add all of these things up as well as the other figures I have given you, that's how you end up in the range of numbers that we have disclosed with the peak forecast. And then ultimately we have also modelled that there may be one or two other novel classes in there but we would expect that the P2X3s get at least 60% of these severe patients.

Nick Stone: Thank you for that comprehensive answer. The next question from Kerry Holford at Berenberg, so Kerry, over to you, please.

Kerry Holford (Berenberg): Thank you, Nick. I have two questions, please. Firstly on depemokimab, given the high potency you've discussed, do you ultimately expect that drug to deliver higher efficacy than *Nucala* and *Fasenra*, or should we really be thinking about that more convenient dosing regimen as the key differentiator to ultimately improving adherence and results in that way?

Then, secondly, I guess my question is on replacement power: today you've discussed what we see as a solid late stage pipeline in respiratory, but I would suggest in contrast that early to mid stage pipeline this disease area at GSK looks relatively sparse, so I wonder if you would perhaps disagree; and whether there are any phase I, phase II respiratory pipeline assets that we should keep an eye on and might be accelerated at GSK? Alternatively, should we be thinking of respiratory as a key area for your business development team considering external opportunities?

Tony Wood: Let me just pick that apart, if I may – let's start with Depe relative to *Nucala* in the first instance. I think the potential advantage on top of the dosing frequency that Luke described is really about compliance, and we're moving to a point where a sense of freedom from the disease is going to be important for these patients, and you saw that to a degree in the video.

I do want to just draw out a distinction, because we haven't had a chance to talk about this yet, between *Nucala* and *Fasenra*. The way I look at the biology here in general - and I'll come on and answer your second question about portfolio and BD in a minute, in the context of this – you can divide it into T2 and low T2 biology. T2 biology is typically that associated with the eosinophilia, and in T2 biology you get to take two options at it – you either go for the cytokine IL-5 or you go for the receptor.

This is the *Nucala/*Depe versus *Fasenra* comparison, and what seems to be the case in this instance that we're learning from the profile that we're developing for *Nucala* is that there is advantage associated with targeting the cytokine because of the deeper tissue effects, and you see that across a range of outcomes when you compare *Nucala* and *Fasenra*, not only with regard to, for example, OCS sparing status in asthma, but also with regard to efficacy in broader eosinophilia. I think we have an advantage in the side of the axis that we've chosen on IL-5 versus the IL-5 receptor, and to your point, bringing in a longer-acting agent is largely going to be associated with compliance.

With regard to the pipeline itself, we have a number of earlier assets coming through that in time we will be able to talk about. I want to stress that we really have focused our efforts, and you can see we have a pretty active phase III pipeline, developing a better understanding of the role of IL-5 in T2

disease in moving the treatment paradigm on for severe eosinophilic asthma, from symptom reduction to exacerbation reduction and ultimately to clinical remission.

One might imagine that you book-end that, for example, in other areas of the biology. We have a TG2 molecule that is in phase I that will allow us to begin to ask questions about the role of development of fibrosis building of top of T2 biology. Alarmins, the other axis of the important biology in lung disease, either from IL-33 or from BD activities in the alarmin class, I won't describe that in more detail, for obvious reasons, also become part of our focus.

So I would say we have a comprehensive programme aimed at positioning new mechanisms in the context of what we're learning about IL-5 in the clinic, and therefore where the most important medical need and opportunity would sit in follow-on agents.

Nick Stone: Thanks, Tony. Can we take our next question from Graham Parry, Bank of America.

Graham Parry (Bank of America): Just a quick question on camlipixant: you talk about the enriched patient population in your phase III study relative to gefapixant, and obviously one of the key things the FDA was saying was they were struggling to see a clinically meaningful reduction. So if you can just help us understand the differences of the patient population in your phase III versus the gefapixant phase III, then the extent to which that then also reduces the addressable patient population from a commercial point of view.

Then secondly, on the *Nucala* COPD study, Dupixent obviously set a very high bar here, 30s reduction but in a narrower patient population arguably. Would you characterise your expectations around *Nucala's* phase III study as being that the inclusion of more emphysema patients broadens your addressable population but perhaps reduces the effect size you are going to see in the study. Thank you.

Nick Stone: Thanks, Graham. Tony, would you like to take the first part of that, and the Luke then over to the *Nucala* question?

Tony Wood: Yes, let's do that. Graham, I'm not going to go into the details of the phase III design because that is something that is still subject to broader conversation with regulators and an aspect of positioning of the agent, and I don't want to share more broadly.

If I could just bring you back to the points that I made earlier, the emphasis for achieving greater treatment effect comes from two broad approaches. The first one is the trial design and that is very much around ensuring that we are admitting those individuals who are more likely to have frequent cough associated with neuropathic origins playing to the mechanism. The higher the frequency of cough, the greater effect one is likely to see, and we look to enrich our patient population with that in mind.

We are also taking account of the fact that there is clearly a placebo effect here, and the greater extent to which one understands the trajectory of that, moving into the study, the greater the opportunity to show a difference.

Then lastly it is probably worth emphasising – because I didn't when I answered the question earlier – that the vastly improved selectivity of dysgeusia will also help confounding features associated with unblinding.

At this point, Graham, I wouldn't want to go any further than that. The only other thing to stress in terms of the regulatory feedback was that there was also commentary on the relevance of the patient-reported outcomes. We have engaged closely with the regulator on that, particularly with regard to the Leicester cough questionnaire, and you will see that accounted for in the relative size of the two phase III populations.

Luke, are you going to do *Nucala*? Go ahead, Luke.

Luke Miels: Thanks, Tony. Graham, all of this was largely visible during the due diligence process with BELLUS as well, because there had obviously been an earlier attempt at approval with gefapixant. As Tony said, if you look at the selectivity, camlipixant is around 1500-fold more selective for P2X3 in contrast to gefapixant, which is three to eight times.

When we did the modelling and the forecasting that you see, and the background to the deal, in the same way as we did with Sierra, we take a conservative assumption in the population and the label, and so the number that you see excludes these milder and non-neuropathic coughing populations. It is very much a severe end of the population, with established extensive disease for more than a year. That is what we have modelled it on.

Just going back to Seamus's question as well, I was just reminded of another analogue that we looked at, which is obviously OFEV IPF analogue, where you saw within three years around 60% of those patients were being treated with a novel agent - a similar prescriber base, high unmet need, difficult disease, etc.

Nick Stone: Just coming back, the question was around *Nucala* inclusion criteria, Tony, for COPD, in terms of Dupi high bar, and whether it was a narrow patient population.

Tony Wood: Let me just make one more point on the PROs for camlipixant as well. They are based on what we have learned from the Ad Com as well, there's a different PRO set as well as a trial design to enable a more extensive demonstration of patient benefit associated with those.

In terms of *Nucala* and the COPD inclusion, you can think about this as follows. We have a broader population, Graham, you are right, and that is aiming for a broader label. It brings a more difficult-to-treat population in the emphysemics, but what we have also done is that we have been careful to enrich that study with regards to eosinophil count, and to be sure we have gone for a purer population of individuals. Both the broader population, if you like, the tougher choice associated with that, has been countered by a more careful selection on the basis of the eosinophils in COPD. We have shown, Graham, that high eosinophilia is associated with poorer outcomes in that COPD population. We are confident, based on the data that we have in that more general population and, indeed as I mentioned earlier, the phase II data in the more bronchitic high-yield population that we have at least equivalent efficacy to Dupi.

Nick Stone: Super, thanks, Tony. Okay, we have two last questions. I am going to come to Ben Jackson at Jefferies first and then I'll finalise with Emmanuel Papadakis at Deutsche Bank, but Ben, over to you in the first instance.

Ben Jackson (Jefferies): Perfect, thank you very much for squeezing me in. Just on camlipixant, I'm aware of the comments that you just made about trial design but I was wondering if there were any further thoughts on the specific comments made by the Ad Com with regard to cough clusters as well as frequency of cough there.

And then I guess off the back of that, are there any thoughts longer term about potentially additional follow-on studies or additional indications that could be gone into from here in the same way that Merck have looked at developing their asset as well? Thank you.

Tony Wood: I'll keep it quick, Ben, and Luke, if you want to pick up on the additional indication comment, I'll make it a quick one.

The way to think about cough clusters is this is all about the analytical method applied to the cough counter. We have taken careful account of that in our interactions with the regulator in terms of the analytical framework that will go forward, so I don't expect to see the desire to recalculate that resulted in one of the trial failures for Merck.

And then with regard to additional indications, one can imagine a number of alternative sensory-afferent based indications like, for example, urinary incontinence which of course is not only a consequence of cough, but a feature of the target patient population here who are likely to be women in their fifties and more, who tend to report with refractory chronic cough.

Luke, I'll hand over to you if you want to embellish on that at all.

Luke Miels: Yes, definitely, and we didn't model those populations in the evaluation of BELLUS, so these are all upside but intend to explore them. Probably less enthusiastic around pain. And then in the chronic cough population, we are planning an extensive post-approval real-world evidence phase IV programme, so, for example, is there an opportunity for primary care doctors to use this mechanism empirically when a patient presents say at eight weeks with chronic cough before sending them off to more invasive or more expensive investigations, even if it's just to attempt to provide some relief, and so there are obviously enormous synergies there with our established infrastructure.

And then we want to do the same thing with depemokimab, back to Kerry's question, because as we have done with *Nucala*, there are opportunities in the real-world setting to demonstrate higher levels of efficacy. In our modelling, we assumed initially at launch in the target medicine profile and all the market research you've seen in these presentations assumes this equivalent efficacy, but we think there is an opportunity in a real-world setting to publish this to assert the benefits of the profile of the drug which could result in better outcomes for patients and a better efficacy claim.

Nick Stone: Thanks, both. Okay, final question to Emmanuel Papadakis, then. Over to you.

Emmanuel Papadakis (Deutsche Bank): Thank you, a couple of quick follow-ups if I may. IL-5s in COPD, given the rerun *Fasenra* study, RESOLUTE in COPD is employing many of the same

modifications that you have made in MATINEE. Is there any reason why we shouldn't assume that will also work, and have you assumed that in your peak sales assumption?

And then a couple of follow-ups on camlipixant. I didn't really understand your comments around the population. The trials are already running, so are you telling us you are discussing with the FDA what precisely will be the population included in the primary endpoint?

And a connected question, apologies if I missed this, are you hoping to show or replicate the 30% approximately placebo-adjusted improvement you saw in the phase II SOOTHE study, or would that only be in a subgroup of the population you have enrolled in CALM-1 and 2? Thank you.

Tony Wood: Let me see if I can clarify that, Emmanuel. First of all, in terms of *Fasenra* and its likely profile in COPD, I'm back to the point I just made to Kerry, that it's important to recognise that across the breadth of performance we see for IL-5 versus IL-5r, IL-5 seems to be the preferred mechanism so I would suggest that if there is a deeper effect associated with disease modification that we might see an improved benefit for *Nucala*, but we will see how that plays out.

In terms of the point that the studies are indeed already running, what I was talking to in that particular comment was the ongoing negotiations we'd had with the FDA during the time period before that study design. What we were keeping in mind there was particularly the point that you make with regard to the distribution of patients who are most likely to benefit from the mechanism – those with higher cough, those adjudicated to have no underlying conditions – and as a consequence of that, aiming to be able to evaluate efficacy across a range of different stratified populations. Then, of course, what we are aiming for there is the sort of placebo-adjusted efficacy that you can see from the phase II study. I would expect to see a range across different populations. All of that is accounted for in the CALM 1 and 2 design.

Nick Stone: Thanks Tony, thanks Luke, especially for highlighting the significant opportunities we have ahead of us. To all of those that have attended, thank you for your interest and attendance. If there are any follow-up questions, don't hesitate to email us at IRteam@GSK.com

With that, we will now close the call. Thank you very much.

[*Ends*]