

GlaxoSmithKline plc
Citi 2017 Global Healthcare Conference
December 7, 2017

Andrew: Terrific. Well look, welcome to the GSK session. I'm with Axel Hoos, who's head of Global Oncology at GSK. You're an interesting spot for a company, which exited oncology only a few years ago and is now rebuilding, although yet to fully commit to a broader oncology franchise. You're presenting some data at ASH with the most advanced of your compounds, with a BCMA ADC. So the abstract is out. Perhaps you could talk to where you see this drug moving to, given a competitive environment with Darzalex and the unique characteristics of the molecule. And then I'll get my breath back whilst we're answering the question, so.

Axel: Well, first of all, thanks for having me. I'm pleased to be back in this kind of environment within an oncology topic for GSK. So I'd like to just correct this perception that GSK has exited oncology. It wasn't a true exit. We had sold our marketed oncology products to Novartis about two and a half years ago and we retained the R&D portfolio. And as Andrew just said, we're rebuilding oncology from that remaining R&D portfolio, which was mostly discovery at the time, two and a half year ago, but it actually has matured now. There's a lot of clinical programs and the most advanced is, as we just heard, the BCMA program, which is an antibody drug conjugate for which we will present the Phase II part of a Phase I/II trial at ASH actually on Monday next week. ASH is beginning at the end of this week and then it leads into the beginning of next week.

So what our BCMA compound represents, and we had actually one public presentation of this before at ASH last year, is the first BCMA targeting agent that has entered the clinic. And as you know, there are three types of molecules being investigated to target BCMA at different stages. One is antibody drug conjugates, the next one is CAR T cells, and the third is bi-specific antibodies.

So the first one that entered the clinic was ours and we have probably the most data around it. Dose escalation is complete. That was what we reported in December last year at ASH. And we now have the cohort expansion complete, which is kind of Phase II data at the recommended Phase II dose, with about 35 patients. The dose we've chosen is 3.4 mg/kg. We have seen about 60% response rate in the last line of therapy in multiple myeloma, with a median progression-free survival of about 8 months.

So if you want to compare that now back to Darzalex, Darzalex, when it was at the same stage of development, had about 30% response rate and about median PFS of close to 4 months. So in that comparison it's about a doubling of the effect

on both counts and we expect that we will have a similar development path going forward where we anticipate to have a launch as a monotherapy in the year 2020. So there will be one more monotherapy investigation after this first in human trial that gets us more data and we would launch with that. That's the projection.

And in parallel, we will expand in two additional tiers to earlier lines of therapy. So there is obviously standard of care combinations with the agents that are dominating the myeloma space in the third and second line, which is proteasome inhibitors, and the EMITs are thalidomide and lenalidomide. We will do those combinations in the early alliance and aim for a label there. And then also in a third tier, combine with immune modulatory drugs, like check point modulators, and we have our own portfolio for that, that would enable a potentially transformation disruptive effect in the myeloma space. And there are staggering valuations going with that, so you're in the few hundred million range for the monotherapy. You go to earlier lines, you might exceed a billion a year, and then you go to several billion if you can actually achieve novel in all the combinations.

Andrew: So thank you for the very full answer because now I've got my breath back, which is terrific. So just stepping back a second and thinking about the overall oncology organization, you now have to build a full scale development program and rebuild the development organization in GSK. I have to think that having the data that you've got with BCMA and the breakthrough status, as well as the augmented hiring that you have been making and now the addition of Hal Barron, that's going to make it much easier for you to attract talent from the experienced myeloma hematology players. Does that make sense?

Axel: That's a fair statement, yes. So, you know, it's a step by step process. Right after the Novartis transaction, many people had the perception that we're really exiting oncology. That certainly made it harder to bring new talent onboard, but to be fair, at that time we didn't need to hire. And now over the last two and half years, hiring needs have increased substantially. We're rebuilding the development organization. Certainly for BCMA, we have to staff up fast. I'm in hiring mode. I have several people that I've brought onboard and we are able to hire again from other premier companies. So as you would expect a big pharma to do. And then as it comes to some very senior level positions, I'm able to announce that we had actually just hired the Oncology Franchise Head, which is my commercial counterpart, to enter the commercial space again with a new oncology compound. That person has just joined us from Novartis, so...

Andrew: Who is that?

Axel: Christine Roth is her name. So this is an announcement actually that was made just today.

Andrew: It's public.

Axel: Good timing. It's public. It's public, yeah, of course. It is public.

Andrew: Just in case Jeff was worried. So the other facet that you have in your emerging hematology business because over the years, I mean you have known heme assets as well with the ICOS and the OX40, but you have some advanced heme assets, the BCMA and then the cell therapies, which you have. So in contrast to your competitors, GSK has been somewhat flying beneath the radar in terms of the focus on cell therapy, and I don't think many investors realize the extent of the infrastructure investments or indeed the magnitude of the treatment effect with some of the very early data, and I'm thinking of again the myeloma data with your NY-ESO. So perhaps you could talk about leveraging the hematology targets through your cell therapies, both on the TCR but also on a CAR T, and give some sense of timelines as to when these agents, sales, may reach the market.

Axel: So I can start with BCMA. For BCMA our projection is, as I think I said it already, is 2020 launch. That would be basically our first commercial product from the new oncology portfolio. If we focus on hematology and actually more specifically multiple myeloma as an area of interest, we have data with the NY-ESO TCR-T, which is autologous T cells that get an affinity mature T cell receptor against the NY-ESO target, which is largely expressed on synovial sarcoma and multiple myeloma and a few other indications.

We have data in both, multiple myeloma and sarcoma. In sarcoma, the response rate is roughly 50% and really good durability. And both FDA and EMA have given breakthrough and prime designation for that. And as you know the NY-ESO program actually originates from Adaptimmune. They have been driving that program. They partnered with us in 2014, and in the last three years we have done co-development. They have operationalized the program and earlier this year we opted in because we reached proof of concept. And this option leads now to a transition of the program to GSK on a platform, as Andrew just said, that we have quietly built over the last five years.

So now we actually started this, and I will revert back to the hematology franchise question in a moment. We have quietly built this in the last five years starting with the rare diseases. And you probably have picked up bits and pieces that we're becoming public over that period. Where we started with Strimvelis as the first marketed cell and gene therapy product for a very rare disease called ADA-SCID, which is an immunological disorder in kids. That only produces about 30 patients a year in Europe. So this was a pilot for us that enabled us to show that we can, from a CMC prospective, actually manufacturer cell and gene therapy products on a GSK platform. This was partnered actually with Telethon Institute in Italy, and then through the regulatory process to actually get a medicine like this to the market. So this was a very effective pilot. Not a commercial opportunity, per se, but an important lesson for us. And we're now expanding from the rare disease space using the lessons we have learned and actually the platform that is scalable and bringing that to oncology. And the Adaptimmune

program will be the first clinical program for oncology that will rest on the new platform.

And if you make a comparison, Novartis has built their cell and gene therapy capabilities. We're in a similar place. There's some differences between what they do and what we do, but in terms of scalability, in terms of depth of science, we're in a similar place to what Novartis has built. We just don't have a commercial product at this point.

So now coming to multiple myeloma or the hematology objective, with BCMA we believe we have an anchor that enables us to work or play in hematology. With NY-ESO, we have seen about an 80% response rate in a post-transplant setting in multiple myeloma. Obviously that data, there's a single arm data that's confounded by the transplant itself, but it still is a clear indicator that this cell therapy works in myeloma. So we have just started another trial in which we will test this alone in a transplant-independent setting where we can more definitively say what the true response rate of the compound is alone and then we will actually do a PD-1 combination to see if PD-1 can enhance the efficacy. And that will give us more knowledge around how we can advance this in the myeloma and maybe the PD-1 combo alone can give us some lessons how we can use PD-1 together with the cell therapy in other places.

Andrew: So turning to the solid tumor targeting therapies you have, we're going to get the first data from the two combinations, I think next year for the ICOS and the OX40?

Axel: We had projected late in 2018 we will have clinical data on combinations with ICOS actually and OX40. But the way we have approached it, and this is actually quite important in my mind, is that we need to be careful how we investigate the next wave of IO agents, which are not as easy to develop as PD-1 blocking antibodies, for example. PD-1 has a great advantage. It produces relatively high response rate across a good spectrum of different diseases. It doesn't work everywhere, but it works in a lot of places.

It's easy to develop, relatively speaking. It's highly competitive. But the other agents that we're now looking at as the next wave are different mechanisms. The highly conserved targets in the immune system, we know they're biologically relevant, but agonists have different kinetics than antagonists. So we need to dissect apart the right patient population, find the right dose, and look for the right combination to really maximize the value of these agents and that is a titrating effort. It doesn't happen overnight. And again, the value comes from finding the right answer, not being fast and eventually too early conclude it's not working.

And I've seen a lot of OX40 work being done that moved really fast and moved under the expectation that OX40 will behave like PD-1. And if you assume that, then it was a big disappointment. It didn't really happen. But if you look at the

biology, it may not be realistic to expect that. So I think we need to dissect it carefully so that we don't conclude failure too early. And that's what we will do. The earliest time we will show data is late '18, but it will depend on what we have at that time for us to decide if this becomes public or not.

Andrew: When you think about the variables and you actually preceded, you answered the question before I asked it, which it's good in terms of setting a frame. But when you think about avoiding the pitfalls, let's just say that Roche may have made in terms of prosecuting OX40, is it a question of dosing that you think that it was just dosed too high and there may be a bell-shaped curve? Is it sequencing because there's some mice data that we've spoken about before that suggests the sequencing with the PD-1 may be important or was it the monoclonal antibody itself or the patient selection? Or is there any signs right now, although you're obviously going to know when you get a full dataset, but is there anything that you can put your finger on which you think is the critical variable?

Axel: So I'm unfortunately not able to give you a definitive answer on this. If we would know we would be there already. So having said that, I think what's critical is dosing, yes. There might very well be a bell-shaped dose response curve. What's critical is the right combination. I don't think that these agonist antibodies or other agonists like TLI agonist, which are now beginning to show clinical activity, but only in combination with other agents. Or even some of the tumor microenvironment agents that have similar kinetics like IDO. Not much immunotherapy activity, but really good synergy with PD-1. So I think we need to look at this in the right combination context.

And then there is a biomarker selection process that we might also want to apply. Tumor mutation burden, for example, is something that's emerging as something of interest. The PD-L1 status we already know in some settings is really relevant. And there are other important biomarkers that are more agent-specific. So if you have T cells that upregulate the receptor that you're targeting with the antibody and the receptors not always present, you might want to look for the expression of the receptor and select your population on that basis before you treat everybody. And the all-comers approach that has been taken so far, which is something you do in dose escalation, hasn't given us all the data yet we need to really pass judgement on this.

Andrew: So you mentioned tumor mutational burden, which is not relation to GSK, but one of your competitors who have written extensively about in terms of how they may be – could be jumping the gun or being pioneers and potentially changing the endpoints of one of their own, going from the controls, despite being not stratified. Stepping back, there is enormous industry activity towards TMB. The recent FDA meeting, approval of two novel tests including TMB assays, and certainly no shortage of datasets showing that it may well be a very useful predictive marker. How are you thinking about that more broadly rather than any particular one program is to something which may well be a good interim stack in

identifying patients who will have all benefit or indeed not have benefit for patient selection? What are the timelines? I mean I would probably say it's going to come sooner rather than later, but if you think it's going to be something that's going to require prospective trials that's only really going to impact in '22, then I'd be interested in hearing your views as well.

Axel: So TMB I think is the next biomarker that revealed itself after PD-L1 for IO agents. And the microsatellite instability, which is a reflection for TMB or a mechanism that can lead to higher mutation load, has already prompted the FDA to make a fairly unprecedented labeling for Keytruda by offering a histology agnostic label, even with some retrospective data to show that this is an important selection marker and that there is potentially a new path for getting new medicines approved if they meet scientifically rigorous criteria around the biomarker.

So I think it prompts the industry, and rightfully so, to look at TMB broadly in a variety of setting for IO agents, of course, but actually also for other agents. I would say we should test the TMB status of cancer patients more generally and enable that knowledge, similar like sequencing the tumor looking for different types of mutations that you can use to target with targeted therapies, to potentially say a patient is eligible for getting an immunotherapy because they have high TMB. So TMB is becoming a relatively important marker and should be available as a piece of information when you select patients for trials and when you do selection of agents to target the disease.

Andrew: When you look at GSK's oncology, diagnostic efforts, given it's not necessarily a strong legacy for you, like it may be for say Roche through their diagnostics division, others have been very overt in announcing the deals that they have done with foundation, with grant, and so on and so forth. Where is GSK along with that journey? Is it just a question of you have not disclosed those relationships and the fact they're already in place or are you actually building up your internal expertise and there's still further work to go, given – I think we're on the same page – that it will shape the treatment path paradigm _____.

Axel: Yes, it will shape the treatment paradigm. Now we had a little bit of a gap after Novartis in terms of having the infrastructure to engage with foundation medicine, for example. The interest for that pre-Novartis existed very clearly and we were in dialogue with them and we did have a companion diagnostic approval for the BRAF inhibitor, dabrafenib that we developed pre-Novartis, which is now marketed by Novartis. So we have been in the area. We have worked on this once before and our expectation is we will yes, as we have a reason to have an assay for any of our compounds that we will be back in that space.

And to be clear, GSK has never stopped working with the community on a variety of programs that can help us advance more generic efforts. So for example, Joe Biden launched the Cancer Moonshot in the middle of last year. GSK was a co-

chair of one of the industry initiatives that were part of the Cancer Moonshot. Actually we were co-chair in one area called PACT, or Partnership for Accelerated Cancer Therapies, which is a biomarker harmonization effort and the clinical trial effort to look for the right combination therapies. That took about almost 18 months, since June last year, to take shape. There was a big industry effort with 12 pharma companies that ultimately committed to it and are co-funding it, together with the government, and it's just launching now. So we're in the contracting phase to commit the resources and it will launch early next year.

So GSK has been a co-chair for that effort. So we never really departed from working with the community and we're doing the same within a project called ATOM, which is also under the Cancer Moonshot, but GSK is the first partner of the Department of Energy and Department of Defense to using their supercomputers to do the drug discovery screening in silico. Instead of high throughput screening with compound in vitro, you would actually feed the computer with the information and let the computer learn and basically do the compound selection in silico. It's a pilot project at the moment, but it helps drug discovery and can accelerate progress in cancer R&D.

So these are just two examples. There are others. But GSK continues to be at the forefront of what the community does. And that will bring us back to once we have a compound that needs a companion diagnostic or we have a compound for which we need to engage in a larger effort like foundation medicine, we will be there.

Andrew: So a question on business development within oncology. So it's two parts. Number one, the relationship you have with Novartis, in our eyes at least, creates and has created many issues for GSK, financial being the main one. But in addition, they have right to first refusal effectively on your clinical pipeline or much of it. So to what extent does that preclude you from entering strategic relationships above and beyond just an R&D collaboration and impedes what you might like to do? So that would be the first question.

The second question is if for Christmas, Emma said, Axel, what would you like in terms of potential acquisitions and targets, what do you think, and what do you think the appetite is for GSK, given all the other constraints on its balance sheet, to prioritize building oncology into something which it wants or aspires to be? Where does it fit in that pecking order of Emma's priorities?

Axel: Nice questions. So I ordered a – I'll answer them in the order you asked. So start with the first one, yes, we are – just remind me of the first question. Sorry. I was answering the second one. I just...

Andrew: The extent to which Novartis' relationship _____.

Axel: So we actually have to be quite explicit about what it means with the remaining component of the deal we did with Novartis, what it actually means. It is a right of first negotiation, emphasis on negotiation, which means at the time when we actually have fileable[sic] data, and BCMA could be the first situation where we encounter that, we will share the data with Novartis. Novartis has the right to place a bid on this or choose not to, and we have the right to accept or reject the bid on this. So there is no obligation on their part or on our part to do anything towards a deal. But it's definitely true, and as it comes up in terms of restriction of any work we can do with others, we've got to go to Novartis first when it comes to a commercialization effort and offer it to them before we can offer it to others. I think that's critical. And then there's one other aspect, which is about good faith negotiations. So if there is – if they're entering into a negotiation, we have to, in good faith, pursue that and we will do the best for GSK and its shareholders in terms of generating value from any potential deal we would do or rejecting a deal if that is in the better interest of the company and its shareholders.

Andrew: But if, for example, you wanted to pick up the phone to your counterpart at let's say, Boehringer, and said, we would like to form a strategic relationship with you. In oncology we think we have synergistic opportunities with our cumulative assets. Unless Novartis agreed to that, that's something that you could pursue.

Axel: That is a good question. So there is a nuance here. So the most important thing I can say is, it's safer to talk to Novartis first than to do stuff alone. So without talking to them, the critical item for me is when it comes to data generation. Since our portfolio is still relatively young, most of what we do is data generation to define directions, including strategic directions. And what we have done so far is we have executed partnerships with other companies to generate data, not strategic alliances to commercialize medicines. But these are development partnerships to generate data, and Keytruda is one example for that. So that is legitimate on the agreement. Once we get to a more mature stage and you want to derive larger and more complex strategic or commercial deals from it, we are well-advised to talk to Novartis first.

Andrew: And then the second question, your Christmas present.

Axel: My Christmas present. So of course I have a wish list, but the wish list will depend a little bit on the changing dynamics that we're about to experience. We hired Hal Barron to become the new Head of R&D. Hal has a great track record as a leader in pharma. He also has a great track record in oncology drug development, so I expect great things from him to come to GSK, but he hasn't started yet. He'll start in January, so it's coming. And I would expect that Hal will influence the way we will think about acquisitions or BD activities. So yes, I have a wish list, but Christmas is before his arrival. So I am not going to push on that Christmas list at the moment. We'll have to just wait until Hal is here and we understand what his vision will be.

Andrew: And since you mentioned Hal...

Axel: And we're doing deals, just to be clear. We have consistently, even after Novartis, even right after Novartis, we have executed business development deals. Adaptimmune is just one example and we have others that are incubating. So there's activity. And you could envision it could pick up with Hal's arrival, but I don't want to preempt that.

Andrew: So, given you've touched upon Hal, he will be based in San Francisco, and yet you have significant number of your research activities based in the UK. There is obviously a lot in the US, but there's also a substantial part in the UK. How problematic do you think that will be, and one assumes that it will require him leaning very heavily on a group of people around him, including yourself, but also lower down inside the organization, to affect the change that he sees. So how much of an operational disadvantage do you see having a geographically remote head of R&D.

Axel: So the first thing I can say is that GSK has made a very concerted effort to establish two major R&D hubs in two parts of the world, one in the UK, one in the US on the East Coast. Those R&D hubs are there to stay. They're not going to move to San Francisco or anything of that, based on what I can tell. And Hal, I would expect, will have to be present commonly in the UK, certainly for governance purposes, but then also to govern and oversee the R&D effort. Yes, he will have to have people on the ground, and I can't fully predict yet how much time he will spend on the West Coast versus elsewhere. That's a dynamic that has to be established. And I have personally not yet spoken to him since he took the role. So everything else beyond what I just said is speculation.

Andrew: I understand. Before we move away from some of the product side, there are a couple of things that we didn't get to. Epigenetics, which is an area where GSK has many, many years of investment, but relatively little still to show in terms of clinical data. And where there has been signs, the agents have moved really quite slowly into registration trials. Now there seems to be some escalation of that or acceleration of that to some of the lead compounds. At the same time, Emma has delineated some of GSK's historic activities as hobbies. So one question is, is epigenetics a hobby and therefore there will be a relative dis-investment in it or is it in that gray zone where it's brimming with promise and therefore it would be foolish to throw in the towel right now and we should allocate time and capital in a very defined way where we think there are very strong possibilities for clinical benefit? Where are we on that continuum?

Axel: So this answer has two components. The first one is GSK has, after Emma's arrival, started a prioritization effort across R&D, which is still ongoing, but some of the fruits of that you have already heard about. We've reduced our therapeutic areas from eight to four, a significant change. We are focused on a variety of programs that we believe have more promise than others and we discontinued

some programs, so there is some activity happening. It may not be the end of it yet, but it was a really important step in the right direction towards directing your resources to what's the more value generating programs. So that's one aspect.

The second aspect is that epigenetics, as a field, is relatively young. GSK got involved in this nine years ago. That's a long time. And we did it right at the time when the DPU model was started at GSK. So the DPU model is a discovery performance unit, which is somewhat of an entrepreneurial discovery unit that sits in R&D. It builds a three-year business plan, gets the business plan funded through a governance review, and then regular check-ins over the period, but it's a three year funding cycle, and they can focus on one specific area of science. So epigenetics has gone through three funding cycles in that nine year period, and I think it has actually generated a lot of important insights biologically, made new compounds, and all of these compounds are small molecules. It has a very broad spectrum of targets that we can now pursue.

We put four molecules in the clinic so far. The first one was a BET inhibitor. Then we had EZH2, LSD1, PRMT5 was the fourth, and there are other PRMTs in that same family actually entering the clinic very shortly. So, of course, you're looking for clinical success. We all do. And I have to say this was an incubation period that we needed to re-understand how these epigenetic compounds work. You have seen how long it took with IO before IO was successful. This was actually a much longer incubation period. And even for ipilimumab, it took 11 years of clinical investigation from first in-human trials to the regulatory approval, and you have seen how much of an explosion it has created in terms of launching IO.

So I'm actually convinced that epigenetics holds the potential to make important medicines. We are now through a large portion of that discovery incubation period. We're learning what happens in a clinic, and to be fair, not all compounds behave the way you want them to. If you look at all-comers, the BET inhibitor, we have treated a lot of patients. We have seen signals of activities in active compound, particularly in diseases that are driven by a BET mutation like NUT midline carcinoma, but it isn't a solution yet. Immunotherapy approach hasn't been the solution, at least for solid tumors, so we moved in synergistic combination settings in prostate cancer and in breast cancer, and that's just for BET. And we have a lot of activity in hematologic malignancies where we see more clinical activity than in solid tumors.

So this is the first wave of clinical investigation with new epigenetic agents. We're now moving to other mechanisms and I'm actually confident. EZH2 has shown 40% response rate, a compound from another company. Ours has shown 20% response rate initially. We have more coming in that area, so meaning more improved compounds. And for the PRMTs, we have seen signals of activity in the dose escalation of the first in-human trials, looked quite interesting. And then when you look at what can you do with these agents? At the end of the game, I

actually think they will all be combination agents to maximize value to be transformational. And pre-clinically where we use certain models to filter what combinations we should do, we know BET inhibitors, at least in our hands, are not behaving well in combination with IO agents.

Andrew: So very different from Novartis’.

Axel: That’s the experience we have made and that seems to be immunosuppressive, at least our compound seems to be. And when you look at the PRMTs, they’re the opposite. They’re immuno supportive and quite synergistic. So as we have an IO portfolio and we have an epigenetics portfolio. Those two would need to be leveraged for synergy and that will also come.

Andrew: So Chris, who use to run that group, has moved on to Rubius. Has his departure and Emma’s narrowing of focus and the messaging that that may have been taken down in epigenetics, has that led to any other departures or key scientist within that organization?

Axel: No, there was no other change. Chris’ choice was voluntary. He wanted to make a new experience and he has done that. We have then actually consolidated our epigenetics efforts. You may know that we had an epigenetics unit in immuno information. We had one in oncology. We brought those two together. That makes the largest DPU in the entire R&D organization to leverage what we have already done and to drive the translation of bringing the biologic mechanisms we understood from the discovery work into the clinic and actually engendered clinical success. That’s where the focus is right now. You’re right, we do need a clinical success. There’s a lot of push in that direction.

Andrew: So going back to BCMA just in the final minutes. You alluded to other modalities targeting BCMA bi-specifics as two or three, maybe more kicking around cell therapy. As you look through some of the emerging data on that, and _____ cell therapy is a little breakthrough designation, the Bluebird, how do you see – first question – the role of CAR T cells, not TCRs, but CAR T cells with the toxicities that bring with them fitting in within an early line myeloma patient population? I struggle to understand where cell therapies end up because I think of it as a Nokia 1980 cell phone. What my iPhone does today is very different from what the Nokia did in 1988. So I don’t know whether cell therapies are on a similar journey and a lot of the issues will be dealt with in 15 years. But I’d be interested in your perspective.

Axel: So obviously cell and gene therapy is a bet that GSK has made. So we believe in it. So I would be dishonest to say I don’t believe in the cell therapies that other people are pursuing. So I see that the CAR Ts for BCMA are meaningful products. They produce good results. And actually from a cytokine release perspective or neurotoxicity perspective, the data I’ve seen, the abstract that was

publicized pre-ASH, actually has less toxicity than had expected. That's a good thing. The response rates are high. So this is very promising.

But there is one, of course, big difference and we are dealing with that with our own cell and gene therapy efforts. There is a question about scalability and the timeline it takes to establish this area, being able to produce at scale larger number of cell therapies for patients. Going from 100 patients a year to 1,000 patients a year to 10,000 patients a year is not a trivial effort. We're at the beginning of that. So this is one item. CMC is a big ticket. And then patient selection is an important item. When you look at the eligibility criteria, GSK, for our BCMA ADC we didn't have to select patients based on a BCMA expression. We took all-comers. The CAR Ts have chosen to look at 50% or more of BCMA expression. That narrows the population you can treat. We have to see how this goes forward as they investigate patients with lower expression.

I personally don't believe, based on any data that I've seen, that the BCMA expression is a major driver of activity. I have to prove that point because we have not selected on it and we have actually not even tested for it. We will go and do that going forward, but we don't have a scalability challenge with an antibody. We don't have a patient selection challenge with an antibody. And we can do clinical investigation much faster. And we're enrolling a trial of 100 patients, will be relatively quick for us. A CAR T approach, given you have to manufacture this individually, it's a very carefully titrated effort and it is a selection process. It will take longer.

And then, of course, it's a matter of how the treating physician will view this. And last year at ASH we had presented our ADC data the very first time. At that time we just came out of dose escalation and in parallel a presentation was given on the CAR Ts. And actually our lead investigator was also the lead investigator on one of the CAR T programs and he actually answered the question from his perspective by saying he would use the CAR Ts mostly in the last line of therapy where he has a defined population, a niche population that he would treat with that, and then antibody is easier to use for a broader and earlier patient population.

And then there is the last point, combinability. We don't know yet how cell therapies will combine with the agents that are established in myeloma, if you go to earlier lines. We don't even know if we need to combine them. We do know that our agent, if you take other antibodies like daratumumab or elotuzumab, as examples, has a high probability of combining well with other therapies. So you can move into earlier lines in the standard way much more quickly.

Andrew: So my final question, last 30 seconds, is we spoke about talent upgrade and talent retention and I'm sure we're going to see a lot of that within the R&D organization. But in addition, there is the motivation and the appetite of GSK to be able to shout about its successes and hopes and aspirations, which historically I think the company has been reticent to do because it's been burned by some very

public R&D disappointments. So obviously Hal's addition to the team is an important part of that. But in general, under Emma's leadership, is there a sense that the self-belief within the R&D organization is already beginning to rise with the additional commitment and the focus, compared to maybe what it has been historically?

Axel: I'm sure that it will rise. In my experience in oncology certainly it is rising. And just the very senior appointments that we made recently with Luke Miels coming from AstraZeneca bringing specialty pharma expertise to commercial; Hal Barron now coming onboard for R&D bringing very focused drug development experience; and actually Laurie Glimcher having joined the board, being the head of Dana-Farber, brings a unique new expertise to GSK on very senior levels that will help us from an oncology perspective to drive our oncology agenda. And it is also quite visible on the outside. It brings people closer to believe when I say, yes, we're in oncology and I'm looking for talent. It's a very helpful situation.

And then, of course, the compounds and the data speak for themselves. BCMA is an attractive compound and I have great talent interest in working on BCMA. And I see it for other compounds, too, but if you work on Keytruda, you work on ICOS. The difference between the two is not science. The difference is Keytruda is established and works, ICOS is at the verge of finding out if it's going to work, so there's a difference in risk profile. But if you want to drive something new in oncology, it's always going to be that way. Whenever the next wave comes, there's always a certain risk associated with that. And the smart people, they know that and they still get excited by the science.

Andrew: So on that note, and I can see the crowd assembling for the next session, Axel, many thanks. Jeff, many thanks for joining us today. Thank you for your interest. Appreciate it.

Axel: Thank you and thanks for your time.

END