LSEG STREETEVENTS

EDITED TRANSCRIPT

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OVERVIEW:

Company Summary

LSEG DATA & ANALYTICS

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Peter Dannenbaum *Merck & Co Inc - Senior Vice President, Investor Relations*

CONFERENCE CALL PARTICIPANTS

Umer Raffat *Evercore Inc - Equity Analyst*

PRESENTATION

Chirfi Guindo - *Merck & Co Inc - Senior Vice President, Chief Marketing Officer - Human Health*

So thank you. We're ready to go.

QUESTIONS AND ANSWERS

Umer Raffat - *Evercore Inc - Equity Analyst*

All right, fantastic. So we'll jump right in. I want to do R&D and commercial. Do we have a preference where we should start?

Chirfi Guindo - *Merck & Co Inc - Senior Vice President, Chief Marketing Officer - Human Health*

Up to you.

Eliav Barr - *Merck & Co Inc - Senior Vice President, Head of Global Clinical Development and Chief Medical Officer*

It's up to you.

Umer Raffat - *Evercore Inc - Equity Analyst*

Okay, we'll start maybe a little bit on the R&D side, and we'll come back to commercial, then probably go back into R&D again.

Maybe in no particular order, let me start with the CADENCE trial, clear success, but it looks like for -- there were these questions around whether it was enough to warrant an FDA submission or at least a regulatory conversation. It doesn't look like it met that bar. Was there a certain number you guys were expecting or a certain end point that would have warranted that? How should we think about that?

Eliav Barr - *Merck & Co Inc - Senior Vice President, Head of Global Clinical Development and Chief Medical Officer*

Yeah, so we're very excited about the CADENCE results because these are patients that don't have any possible, any current, therapy to improve their outcomes and their ability to engage in activities of daily living. These are patients who've got pre and post capillary, pulmonary hypertension caused by heart failure with preserved ejection fraction. So it's a really discreet but very important population.

And the results were really quite good. We're very happy with them. This was a proof-of-concept study, so it's not a regulatory, it's not a filing study, but it gave us rock-solid evidence that we can move on to Phase III.

We think this is really going to be important for patients -- we look forward to seeing the results being presented in upcoming meetings so that everyone can assess it. Our steering committee has been super happy about it, and we're going to head to Phase III in 2026.

Umer Raffat - *Evercore Inc - Equity Analyst*

Got it. So is this a launch which is post 2030?

Eliav Barr - *Merck & Co Inc - Senior Vice President, Head of Global Clinical Development and Chief Medical Officer*

I can't -- I don't know. And the reason why I don't -- I don't mean to not answer the question, it's just we have to figure out what the primary endpoint is going to be for Phase III, and that requires discussions with our steering committee, our regulatory agencies and so on.

Umer Raffat - *Evercore Inc - Equity Analyst*

I see. I see. Is it fair to say that there is a signal on time to clinical worsening?

Eliav Barr - *Merck & Co Inc - Senior Vice President, Head of Global Clinical Development and Chief Medical Officer*

We didn't -- we haven't disclosed other endpoints, but I would tell you that we're confident that we can move to Phase III.

Umer Raffat - *Evercore Inc - Equity Analyst*

Got it. When I did some checks on this, one of the feedbacks I was hearing quite often was part of the reason Phase II took so long to recruit was because the inclusion was very restrictive on the Wood units involved more than 4. Would Merck look to relax that?

Eliav Barr - *Merck & Co Inc - Senior Vice President, Head of Global Clinical Development and Chief Medical Officer*

One of the axioms that I've learned through bitter experience is don't get a Phase III signal that looks really good and then go ahead in Phase III and change everything, because that just doesn't make sense, particularly when you have a new biology like the story here. I actually think that the reason why enrollment took so long to begin with is because no one looks for these patients at present because there's nothing to give them.

And I recall back in my days with hepatitis C, the moment we started to see patients with -- to see the promise of the new therapies, everyone came out of the woodwork to be retested and be ready. I see this as a similar sort of thing. Once you start -- once you have something that you can offer to people, then people are testing, will test for it.

And for me, we saw that at the -- in the last months of enrollment, all of a sudden there is a lot of interest once they saw the results of ZENITH, in STELLAR. They said, maybe this is good for my patient. And all of a sudden, patients showed up. So we had a big acceleration of enrollment. So I see Phase III enrolling quickly even with this --

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Umer Raffat - *Evercore Inc - Equity Analyst*

Got it. Chirfi, maybe just taking that enrollment to the commercial side, I guess one thing that confused me on CADENCE was it was about 160 patients, but it took 120 sites to deliver 160 patients. Does that form a very tough commercial uplift? Or do you think it will be very different once the data are out there?

Chirfi Guindo - *Merck & Co Inc - Senior Vice President, Chief Marketing Officer - Human Health*

Yes. So the CpcPH population we estimate to be roughly the same size as PAH. So you're thinking about -- you're looking at [40,000 to 50,000] (corrected by company after the call) in the United States.

But as Eliav mentioned, the diagnosis rate is lower because physicians have not been looking for it. And so we think that, again, post-Phase III data, once people start to see the presentation next year of the Phase II, right, more physicians will be sensitized and look CADENCE patients. So we don't anticipate a different commercial model to what we have with PAH, and we will be able to execute this.

Umer Raffat - *Evercore Inc - Equity Analyst*

Got it. Your confidence on WINREVAIR sotatercept trajectory right now remains good. I know there were some questions a couple of quarters ago on whether rate of patient adds was slowing, but it sounds like things are pretty smooth.

Chirfi Guindo - *Merck & Co Inc - Senior Vice President, Chief Marketing Officer - Human Health*

Absolutely. And then our confidence is growing because the data with ZENITH and HYPERION now, what you're seeing is, in the US, just to stick to the US for a moment, the majority of our patients have come from the more severe PAH cases, right? So about 75% of those new patients starting on WINREVAIR in the US.

And so those are triple therapy patients. But we're seeing an increasing willingness by physicians to treat the less severe patients. And so the data from HYPERION, in particular, is giving confidence. So we are going to see a steady growth, [400 to 500] (corrected by company after the call) patients steady every month coming into treatment with WINREVAIR.

And then we're launching outside of the US. We're very encouraged by the early signals from Japan, and we're going through the reimbursement process, in Europe, you know that it takes longer typically. But the feedback has been tremendous across.

Umer Raffat - *Evercore Inc - Equity Analyst*

Fantastic. Fantastic. Which takes me then to another important launch from Merck next year, PCSK9. I think Peter would tell you, the Street has a lot of questions on this one in terms of is this a real launch or not. Obviously, the Merck opinion is very different than the Street opinion on this.

So maybe this is a question first for you, Chirfi. I'm sure Rob has a number out there for you to deliver on this. But is the feedback you're hearing from AHA consistent with sort of the perception that the broader organization has?

Chirfi Guindo - *Merck & Co Inc - Senior Vice President, Chief Marketing Officer - Human Health*

We are not surprised by the feedback. I was at --

Umer Raffat - *Evercore Inc - Equity Analyst*

Which one. The investor feedback or?

Chirfi Guindo - *Merck & Co Inc - Senior Vice President, Chief Marketing Officer - Human Health*

AHA.

Umer Raffat - *Evercore Inc - Equity Analyst*

Doctor feedback. Okay.

Chirfi Guindo - *Merck & Co Inc - Senior Vice President, Chief Marketing Officer - Human Health*

Thanks for clarifying. I mean we're really excited about the opportunity of enlicitide. I mean this is potentially a game changer, right? There's a cardiovascular epidemic going on, right? So despite all the tools that are available, the injectable PCSK9s have not really had the kind of impact that was anticipated, given how powerful they are really.

The whole mechanism is just such an incredible. So to be able to deliver a PCSK9 antibody efficacy in a pill form, right, and I summarize it as 60, 50, 50 30, when you think about the efficacy of enlicitide. 60% reduction in LDL cholesterol, 50% reduction in non-HDL cholesterol, 50% reduction in ApoB and 30% reduction in LP(a). I mean that's the profile that was presented at AHA. And that was really surprising to the scientific community. And so not to us, but to the scientific community certainly.

And then the AE profile, comparable to placebo. So think about that. And that's a really, really big deal. We think that we now have a tool that will allow us to democratize access, and so to really, really drive LDL lowering in the US and around the world.

Umer Raffat - *Evercore Inc - Equity Analyst*

So I want to come back to access because I've been getting questions on it lately as well. But just before that, the feedback on food effect, feedback on sort of drug, drugs, you can't take multiple drugs together. Like how --

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Chirfi Guindo - *Merck & Co Inc - Senior Vice President, Chief Marketing Officer - Human Health*

Yeah. So no, thanks for the question. So drug-drug interaction does not appear to be --

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Umer Raffat - *Evercore Inc - Equity Analyst*

Yeah. Can you take other meds with it, like the blood thinners and all that?

Chirfi Guindo - *Merck & Co Inc - Senior Vice President, Chief Marketing Officer - Human Health*

So that's a big deal. That's a big deal.

Eliav Barr - *Merck & Co Inc - Senior Vice President, Head of Global Clinical Development and Chief Medical Officer*

Yes. No issues there.

Chirfi Guindo - *Merck & Co Inc - Senior Vice President, Chief Marketing Officer - Human Health*

That's a big deal. And then the food effect in the study, and Eliav can talk to it, but 97% of patients in the program were able to follow the regimen. You take it in the morning, 30 minutes later you go about your breakfast, not an issue at all. And so again, the scientific community was ecstatic.

Eliav Barr - *Merck & Co Inc - Senior Vice President, Head of Global Clinical Development and Chief Medical Officer*

For us, what was really interesting was the lack of any -- it was kind of let's talk about how we're going to implement as opposed to worry about this sort of things. A, lack of DDI, consistency of effect that was really exciting for people.

Umer Raffat - *Evercore Inc - Equity Analyst*

Got it. What -- Peter, I think there was a comment shared on the transcript recently, and I'm not sure if you could chime in as well, on access. There's this perception that you guys are looking to come in below where the current PCSK9 unbranded pricings are. I just want to make sure I understand exactly what you guys are doing.

Peter Dannenbaum - *Merck & Co Inc - Senior Vice President, Investor Relations*

Yeah. We've not been that specific. We've just said we're going to price for access for broad access. And we've not been specific with respect to what that means in terms of gross or net prices.

Umer Raffat - *Evercore Inc - Equity Analyst*

I see.

Chirfi Guindo - *Merck & Co Inc - Senior Vice President, Chief Marketing Officer - Human Health*

We do not anticipate price to be a barrier. I mean we are going to price appropriately for value and for access. We really want to drive rapid access. I mean just to be clear, I mean, we are going to need guidelines to be updated, right?

And so as you think about the models that we are working through internally, we're going to need to activate the inertia that exists in the space, I'm sure that guidelines are updated, so that more patients can benefit from the power of enlicitide.

Eliav Barr - *Merck & Co Inc - Senior Vice President, Head of Global Clinical Development and Chief Medical Officer*

And interestingly, the VESALIUS study results are, I think we're a major recipient of benefit of that, being able to show tremendous reduction in cardiovascular outcomes in patients who are higher -- or primary prevention patients is going to be very, very useful. It's the place where cholesterol management is done. And I think that that's going to be very useful for --

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Umer Raffat - *Evercore Inc - Equity Analyst*

Right. There's another oral cholesterol launch next year as well. Is that factoring into your expectations somewhere? Do both of these launches just do well, both new cholesterol offerings? I realize that's a different mechanism, but a lot of LDL reduction from New Amsterdam.

Chirfi Guindo - *Merck & Co Inc - Senior Vice President, Chief Marketing Officer - Human Health*

Yeah. So I mean, obviously, as you said, it's a different mechanism of action. I think the excitement really is around oral PCSK9. It's such a powerful -- we believe we'll have the most powerful LDL-lowering oral agent either on the market or in development, period. So we'll be well differentiated.

Umer Raffat - *Evercore Inc - Equity Analyst*

Okay. Fantastic. Maybe perhaps then moving on to some of the other programs, I want to start to get into oncology a little bit. TROP2-ADC, your expectations in the EGFR mutant lung and HR-positive breast, especially in light of some of the underwhelming findings from the Gilead side in both those indications, just in lung broadly as well as HR-positive breast as well.

Eliav Barr - *Merck & Co Inc - Senior Vice President, Head of Global Clinical Development and Chief Medical Officer*

Sure. So ADCs are very unique. Each one of them is different. They're different in every element of the -- so with Gilead, of course, the antibody is the same, but we have a very different linker, we have a different dosing strategy, a very different development approach, et cetera. So I don't think you can read through positively or negatively from one to another.

We've chosen a very specific dosing strategy and a specific approach that leverages the reliable efficacy and the easy to detect and treat safety profile of sac-TMT. The idea here is to have a workhorse drug that's available for both the NCI cancer center and the community practitioner oncologist. That's why we have a broader spectrum of diseases that we're evaluating. That's why we're putting a lot of things with pembro. That's why we are very GYN forward, maintenance forward, et cetera.

So I think that that -- all this is a very differentiated profile. So I wouldn't read too much on what Gilead has done to address what we have in our pipeline. What I would though say --

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Umer Raffat - *Evercore Inc - Equity Analyst*

But the payload doesn't matter in your opinion, lung setting?

Eliav Barr - *Merck & Co Inc - Senior Vice President, Head of Global Clinical Development and Chief Medical Officer*

We have -- our payload is really quite effective in lung. And how I know that, I know that because there's two studies now that are floridly nicely positive with Kelun in China. The first is OptiTROP-04, which was actually presented and is published. And then very recently, OptiTROP-05, which was presented top-line results by Kelun -- and to me, is a very significant -- that study is a very significant study because it's sac-TMT plus pembro.

And I think that these data really validate why we think sac-TMT is different. And the right -- that right sweet spot for patients with good activity, in some cases, biomarker defined, a safety profile that's easily manageable, long durations of therapy, and again, it allows us to -- it will -- and settings where that benefit is not clouded by having to go up against platinum chemotherapy, which is really great. It's good chemotherapy, and on the background of pembro.

Umer Raffat - *Evercore Inc - Equity Analyst*

Fantastic. Fantastic. Is there a possibility that we get some sort of an interim look on your EGFR mutant lung study and or perhaps even the HR-positive breast study next year?

Eliav Barr - *Merck & Co Inc - Senior Vice President, Head of Global Clinical Development and Chief Medical Officer*

So we don't share when -- we always have interim analysis in all of our studies. The PCD dates are the most -- are the ones that investors typically look at. We do have interim analyses, will be event driven, so I really can't say exactly when and where.

But remember, we've got 15 Phase III studies that are ongoing, 10 of which are novel settings. They're all enrolling like nobody's business, which is always a leading indicator, for me, a leading indicator of enthusiasm. And so they'll come when they come.

Umer Raffat - *Evercore Inc - Equity Analyst*

Right. Fair to say there haven't been any interims passed on those, because it's too early for that.

Eliav Barr - *Merck & Co Inc - Senior Vice President, Head of Global Clinical Development and Chief Medical Officer*

It's early. We do things like futility, but that's not really an efficacy. Like those are easy-peasy ones.

Umer Raffat - *Evercore Inc - Equity Analyst*

Okay. Got it. But that would have been a big surprise if there was a futility.

Eliav Barr - *Merck & Co Inc - Senior Vice President, Head of Global Clinical Development and Chief Medical Officer*

Yeah.

Umer Raffat - *Evercore Inc - Equity Analyst*

Okay. Eliav, I know I've talked about this with you a couple of years now. The BTK inhibitor. Lilly is on the market now. Merck is going to market at some point. I guess, when would that be? Could there be some sort of readout possible in '26? CLL?

Eliav Barr - *Merck & Co Inc - Senior Vice President, Head of Global Clinical Development and Chief Medical Officer*

Yes, what we've done with nemtabrutinib is gone for that long path that's going to just get us to the touch down earlier than everyone else. But what I mean by that is to take everything and put it on the frontline.

Umer Raffat - *Evercore Inc - Equity Analyst*

Okay. You do the refractory for dose?

Eliav Barr - *Merck & Co Inc - Senior Vice President, Head of Global Clinical Development and Chief Medical Officer*

We have refractory, but it's -- it will come right at the same time. The front line -- because that's where the action is, right? That's where patients will get benefit. You want to be able to give people a drug that you can use for long periods of time and you won't get mutations. So nemtabrutinib has got the highest barrier to resistance because it's got a little bit of other non-BTK activity. And what we've chosen to do is to take it right into the front line.

And unlike the other studies which is frontline plus, so not really front line, and not designed for the hard endpoints, we have a much larger study that's enrolled and now we are following patients up. And it's going to be mostly against acalabrutinib, very little like ibrutinib. And so it's going to be a very straight up comparison.

So we'll see what happens. But I'm confident that nemta will be -- that we'll be able to see the results and be able to show benefit. If our hypothesis is right, we'll be able to demonstrate non-inferiority and potentially superiority and lack of resistance. I think that's the key.

Pirto have shown some data on what the resistant profile is. And we looked at our data and we saw that our drug would have been able to overcome resistances, where pirto resistant, doesn't -- it remains -- I mean, it becomes inactive.

Umer Raffat - *Evercore Inc - Equity Analyst*

Got it. I guess how do you think this trial could differentiate over Lilly's pirtobrutinib 313?

Eliav Barr - *Merck & Co Inc - Senior Vice President, Head of Global Clinical Development and Chief Medical Officer*

Because it's straightforward first line. I mean it's not a -- and it's -- the endpoints are different. We start with non-inferiority, but then we go to superiority and then we go to --

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Umer Raffat - *Evercore Inc - Equity Analyst*

Could there be a clinical profile difference?

Eliav Barr - *Merck & Co Inc - Senior Vice President, Head of Global Clinical Development and Chief Medical Officer*

Yeah, maybe. We'll see. That depends on the Phase III trial. I really can't -- I mean, we put all of our efforts into doing that with the idea that there would be a different clinical profile. We chose something a little dirtier because we thought that -- when I say a little dirtier, I mean a little more -- other receptors that it binds, tyrosine kinase inhibitors that it also inhibits, with the idea of having a little extra efficacy.

Now the trade-off is whether there's going to be a safety profile difference. We don't know. But the data looked pretty good so far in blinded fashion.

Umer Raffat - *Evercore Inc - Equity Analyst*

Got it. But just so I'm clear, the BRUIN 313 for pirtobrutinib, that was a clean first-line study, no?

Eliav Barr - *Merck & Co Inc - Senior Vice President, Head of Global Clinical Development and Chief Medical Officer*

Not exactly. It was a smaller study. It didn't have the long-term outcomes.

Umer Raffat - *Evercore Inc - Equity Analyst*

You mean on OS?

Eliav Barr - *Merck & Co Inc - Senior Vice President, Head of Global Clinical Development and Chief Medical Officer*

Yeah. Right.

Umer Raffat - *Evercore Inc - Equity Analyst*

Got it. Excellent. So maybe moving on to a program everybody cares about a lot, which is PD-1 VEGF.

Eliav Barr - *Merck & Co Inc - Senior Vice President, Head of Global Clinical Development and Chief Medical Officer*

Oh, that one.

Umer Raffat - *Evercore Inc - Equity Analyst*

What's the -- I guess, let me ask you this. If it shows what the other PD-1 VEGFs have shown, which is about a 50% to 60% response rate, given what we know on overall survival data for the rest of the programs, is Merck going right into some sort of Phase II registrational? Or is this going to be more slower than that?

Eliav Barr - *Merck & Co Inc - Senior Vice President, Head of Global Clinical Development and Chief Medical Officer*

So the challenge with PD-1 VEGF is to show that PFS translates to OS. It's the age-old question. We've had a little initial possibility in China. We'll see if that's really true. The issue with that is that the delta between the PFS hazard ratio and the OS hazard ratio was pretty gargantuan. Europe, something at 0.5, and then something like 0.78, which was kind of you wonder why. And so we have to wait and see.

So for us, it's a disciplined approach. We have MK 2010 that's from LaNova. It's very active. It looks good. And ORR is a good marker for choosing dose, but it's not -- doesn't -- won't tell you if you're going to ultimately improve overall survival. And that's where the discipline comes in.

And you'll see some of those apropos sac-TMT, it'd be very interesting for investors to look when Kelun finally presents the results of OptiTROP-05 to compare that to HARMONi-2 and ask the question, how does that -- how do the two compare? And what does that mean?

And so -- but we're interested in PD-1 VEGF, and we're interested in it in a disciplined way. And I think it's -- we have to say the proof is in the pudding, and not fall into the pitfall that we fell in. Because I can tell you, it's me, I was the one that invested in pembro-lenva and had a success rate that wouldn't get me anywhere near the big leagues.

Umer Raffat - *Evercore Inc - Equity Analyst*

So it sounds like you're much more guarded on PD-1 VEGFs this year than. --

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Eliav Barr - *Merck & Co Inc - Senior Vice President, Head of Global Clinical Development and Chief Medical Officer*

No, no. Just -- yes.

Umer Raffat - *Evercore Inc - Equity Analyst*

Has it always been like that, or do you feel like that even more after --

Eliav Barr - *Merck & Co Inc - Senior Vice President, Head of Global Clinical Development and Chief Medical Officer*

It's always been that way, but --

Umer Raffat - *Evercore Inc - Equity Analyst*

You're more open about it now.

Eliav Barr - *Merck & Co Inc - Senior Vice President, Head of Global Clinical Development and Chief Medical Officer*

Just I feel like I'm waiting all the time. It's -- no. No not quite.

Umer Raffat - *Evercore Inc - Equity Analyst*

Can I ask you a controversial question then?

Eliav Barr - *Merck & Co Inc - Senior Vice President, Head of Global Clinical Development and Chief Medical Officer*

Yeah.

Umer Raffat - *Evercore Inc - Equity Analyst*

There's an IO-IO combo, which had a second interim OS of 0.81. And we know PD-1 VEGFs have second interim OS of 0.78. That first IO-IO of 0.81 was PD-1 TIGIT and the 0.78 is PD-1 VEGF. But the perception from the Street is very different between those two combos. I guess, how do you think about that?

Eliav Barr - *Merck & Co Inc - Senior Vice President, Head of Global Clinical Development and Chief Medical Officer*

Beware.

Umer Raffat - *Evercore Inc - Equity Analyst*

Okay. Okay. And let me take it to another extreme then. Is it possible that these PD-1 VEGFs are just a high-dose PD-1?

Eliav Barr - *Merck & Co Inc - Senior Vice President, Head of Global Clinical Development and Chief Medical Officer*

Possible, but they -- well, not quite because they also have the AEs profile of VEGF, some --

Umer Raffat - *Evercore Inc - Equity Analyst*

Sure. But my point is, is the efficacy simply the higher PD-1 driving adverse --

Eliav Barr - *Merck & Co Inc - Senior Vice President, Head of Global Clinical Development and Chief Medical Officer*

I'd ask the other question -- a little different question. I'd say, if you take KEYTRUDA and you add Avastin, and then you compare it to PD-1 VEGF, is there any difference in efficacy? That would be an interesting question.

Because the concept is that by somehow having it on the same molecule, you've done something really biologically different. There is a daisy-chain concept that people are talking about. There's the increased internalization. There's the being able to intensify the immune modulation, or something of that nature. And yet there's been studies that have looked at PD-1 and VEGF, and you see PFS benefit. We just don't see much of an OS benefit, is all.

Umer Raffat - *Evercore Inc - Equity Analyst*

Got it. So it sounds like you want to see a definitive OS signal before you commit any significant resources here.

Eliav Barr - *Merck & Co Inc - Senior Vice President, Head of Global Clinical Development and Chief Medical Officer*

We're going to commit it in a stage way. I'm not -- I don't want to talk through all the different if-thens. Some of it has to do with the drug, some of it has to do with the drug plus other drugs that we have in our pipeline.

Umer Raffat - *Evercore Inc - Equity Analyst*

And Eliav, could you remind me the trial that LaNova was running. It was, I think, 200-plus patients, but it got cut into half right ahead of their sale, what happened there?

Eliav Barr - *Merck & Co Inc - Senior Vice President, Head of Global Clinical Development and Chief Medical Officer*

Because we took out the drugs that were -- the combos with drugs that they -- with drugs that we didn't buy from them. There are arms with other LaNova products, and then so -- and then we didn't need that. And so -- and we're going to globalize after this trial.

Umer Raffat - *Evercore Inc - Equity Analyst*

Got it. Do you have a US IND on this drug?

Eliav Barr - *Merck & Co Inc - Senior Vice President, Head of Global Clinical Development and Chief Medical Officer*

Not yet, but it's coming.

Umer Raffat - *Evercore Inc - Equity Analyst*

Okay. And why the delay? Because it sounds like there's enough data to warrant it.

Eliav Barr - *Merck & Co Inc - Senior Vice President, Head of Global Clinical Development and Chief Medical Officer*

Because it's -- we've got a lot of stuff that we're able to do in China. Right now, our -- we have a pretty vast footprint there, and Phase I data, hopefully, the US will change its point of view, make Phase I easier in the United States. But China is easy to work with.

Umer Raffat - *Evercore Inc - Equity Analyst*

Got it. So this is a question for Chirfi then. If the Summit Akeso programs have an overall survival of, let's say, 0.84 final OS, do you think that type of profile warrants a potential KEYTRUDA life cycle management within Merck where you could do a big switch over to an internal program? Is that to breach threshold enough to do that?

Chirfi Guindo - *Merck & Co Inc - Senior Vice President, Chief Marketing Officer - Human Health*

It's very difficult to comment. I mean you have to look at specific tumor types. You have to look at the standard of care per tumor type. And really, the bar has been set in each one of those. I mean that's what will drive adoption ultimately. So it's difficult to give you --

Umer Raffat - *Evercore Inc - Equity Analyst*

Okay. So it's -- but like let's say lung in particular, if there's like a 0.84 hazard ratio, could a Merck's in-house PD-1 VEGF effectively replace KEYTRUDA in lung with that type of hazard ratio? Or is that not enough?

Chirfi Guindo - *Merck & Co Inc - Senior Vice President, Chief Marketing Officer - Human Health*

I would -- again, I would reserve my answer on this one. I would not --

Umer Raffat - *Evercore Inc - Equity Analyst*

So the base case plan for the company is not to sort of plan some sort of switch internally to an incremental program?

Chirfi Guindo - *Merck & Co Inc - Senior Vice President, Chief Marketing Officer - Human Health*

Yes. Not a wholesale switch. This would have to be really tumor dependent.

Umer Raffat - *Evercore Inc - Equity Analyst*

I see. Peter, I think you were going to say something on this?

Peter Dannenbaum - *Merck & Co Inc - Senior Vice President, Investor Relations*

No.

Umer Raffat - *Evercore Inc - Equity Analyst*

Okay. Great. One more on an IND topic we discussed last year, the oral GLP from China. I feel like that's been in the preclinical for a while. It looks like there wasn't enough preclinical done on the Chinese side before it was brought in. So I'm just curious --

Eliav Barr - *Merck & Co Inc - Senior Vice President, Head of Global Clinical Development and Chief Medical Officer*

Hold on. It's coming.

Umer Raffat - *Evercore Inc - Equity Analyst*

Okay. All right. I always get a sense sometimes when I listen to Dean that the interest is much more on making acyclic peptide, which is a true sort of oral synthetic peptide rather than a small molecule. So this may not be the top priority for all GLPs. Is that true or --

Eliav Barr - *Merck & Co Inc - Senior Vice President, Head of Global Clinical Development and Chief Medical Officer*

No, I don't think that that's necessarily true. I think what Dean is talking about is the power of macrocyclics to be able to have antibody-like effects like what we've seen with enlicitide. I think he's really excited about the technology. Now we wouldn't have bought MK-4082 if we weren't interested in MK-4082.

Umer Raffat - *Evercore Inc - Equity Analyst*

Got it. I want to transition to ophthalmology franchise, and then I want to talk about immunology as well. John Reed is in the audience, so we'll talk about J&J pipeline. Competitive feedback. But let me start with EyeBio for a quick second. Chirfi, how big an indication is that? And with two shots in the eye, like can you just frame that for us?

Chirfi Guindo - *Merck & Co Inc - Senior Vice President, Chief Marketing Officer - Human Health*

Yes. So we're really excited about the EyeBio acquisition, and the program is advancing really, really rapidly, which as Eliav mentioned earlier, is always a sign of enthusiasm in the community when you are enrolling very rapidly.

So just for context, obviously, anti-VEGFs are the standard of care in DME as well as wet AMD. But we have -- the insights we're getting from the community is that up to 40% of patients are really not well controlled or not responding at all to anti-VEGFs standard of care. So there is an unmet medical need here. And so there's a need for new MOAs.

And so this is what really the EyeBio acquisition affords us. MK-3000 is a Wnt agonist, a new MOA. And then you have Tiespectus, which is a bispecific of Tie-2 and VEGF. And so the combination of those two really will address this high unmet medical need that I just talked about. And --

Umer Raffat - *Evercore Inc - Equity Analyst*

But docs are comfortable with two separate shots in the DME setting?

Chirfi Guindo - *Merck & Co Inc - Senior Vice President, Chief Marketing Officer - Human Health*

So there is a trend in this community towards personalizing the treatment, right? So this is, as you do your programs, as you do your studies, you typically have your more frequent injections. And then over time, we've seen that with all the retinal disease, all the launches in retina over the past number of years, over time, with additional data, the frequency of administration goes down in the real world.

So the same will happen here for MK-3000 and Tiespectus. At the end of the day, it's about the efficacy. It's about the new MOA that we're bringing to market. And really, really exciting.

Umer Raffat - *Evercore Inc - Equity Analyst*

Is this a multibillion opportunity?

Chirfi Guindo - *Merck & Co Inc - Senior Vice President, Chief Marketing Officer - Human Health*

Totally. Yes.

Eliav Barr - *Merck & Co Inc - Senior Vice President, Head of Global Clinical Development and Chief Medical Officer*

Just real quickly. We're talking about one injection. We're not talking about --

Umer Raffat - *Evercore Inc - Equity Analyst*

No, the VEGF still happen, no?

Eliav Barr - *Merck & Co Inc - Senior Vice President, Head of Global Clinical Development and Chief Medical Officer*

No. The Wnt is being administered separately as monotherapy.

Umer Raffat - *Evercore Inc - Equity Analyst*

As monotherapy? And these are naives as well?

Eliav Barr - *Merck & Co Inc - Senior Vice President, Head of Global Clinical Development and Chief Medical Officer*

Naives and people who have failed.

Umer Raffat - *Evercore Inc - Equity Analyst*

I see. So there's no concurrent VEGF injection?

Eliav Barr - *Merck & Co Inc - Senior Vice President, Head of Global Clinical Development and Chief Medical Officer*

There's like a couple of a small arm of patients. But I think the -- for people who might benefit from VEGF, that's where Tiespectus or MK-8748 would be . It's only going to be one shot at a time.

Umer Raffat - *Evercore Inc - Equity Analyst*

Got it. Eliav, when I looked at the prior data, I think that was the AMARONE study, the confidence intervals looked very, very wide. And I wondered, is that just like very high dispersion around what different patients were doing? Or was that just like very tiny and --

Eliav Barr - *Merck & Co Inc - Senior Vice President, Head of Global Clinical Development and Chief Medical Officer*

It's a small n thing. I think that the results were actually pretty consistent. The CST results were quite consistent across the board and over time in that 12-week study. Remember, it's just 12-week study, it's not a 1-year study, where eventually people who are slower responders eventually get there. So no, we're not worried about that at all.

And both the BRUNELLO trial is nearing completion and BAROLO afterwards. So I think we'll have good results and good data on Wnt.

Umer Raffat - *Evercore Inc - Equity Analyst*

Okay. So it was not like patients with low CSTs did better and -- it was fairly consistent.

Eliav Barr - *Merck & Co Inc - Senior Vice President, Head of Global Clinical Development and Chief Medical Officer*

It was fairly consistent across the board.

Umer Raffat - *Evercore Inc - Equity Analyst*

Got it. What about the -- and I've been burned by this on a couple of companies I cover in the retina space. But can you speak to intraocular inflammation, vasculitis?

Eliav Barr - *Merck & Co Inc - Senior Vice President, Head of Global Clinical Development and Chief Medical Officer*

Nothing yet.

Umer Raffat - *Evercore Inc - Equity Analyst*

That community is very intense, even on one case. So nothing -- no observations?

Eliav Barr - *Merck & Co Inc - Senior Vice President, Head of Global Clinical Development and Chief Medical Officer*

Not yet.

Umer Raffat - *Evercore Inc - Equity Analyst*

Okay. Got it.

Eliav Barr - *Merck & Co Inc - Senior Vice President, Head of Global Clinical Development and Chief Medical Officer*

I mean clinical studies go on.

Umer Raffat - *Evercore Inc - Equity Analyst*

Got it. What about rescue criteria, how does that work in the setting?

Eliav Barr - *Merck & Co Inc - Senior Vice President, Head of Global Clinical Development and Chief Medical Officer*

So the protocol, there's a rescue criteria for people, they have recommendations for different kinds of progressions that occur both in terms of what they see in the eye and then drops in letters. It's at the end of the day up to the physician to figure out what she or he wants to do with that patient. But they do have some rescue events -- some rescue methodology that's available. I don't know what the numbers look like simply because it's blinded.

Umer Raffat - *Evercore Inc - Equity Analyst*

Got it. Peter, would you remind us the timing on this readout for next year?

Peter Dannenbaum - *Merck & Co Inc - Senior Vice President, Investor Relations*

Ophthalmology is toward the end of next year, the first trial, right?

Chirfi Guindo - *Merck & Co Inc - Senior Vice President, Chief Marketing Officer - Human Health*

Yeah. That's DME.

Peter Dannenbaum - *Merck & Co Inc - Senior Vice President, Investor Relations*

Yeah.

Eliav Barr - *Merck & Co Inc - Senior Vice President, Head of Global Clinical Development and Chief Medical Officer*

That's going to be the BRUNELLO trial.

Umer Raffat - *Evercore Inc - Equity Analyst*

DME. And the Tiespectus is the year after, correct?

Peter Dannenbaum - *Merck & Co Inc - Senior Vice President, Investor Relations*

Phase II Tiespectus will be next year as well.

Umer Raffat - *Evercore Inc - Equity Analyst*

Phase II Tiespectus next year. Makes sense. Okay. Great. Perhaps we can just keep moving here.

And maybe just a quick reminder, what about AMD? Is that a consideration for Merck as you went into retina?

Chirfi Guindo - *Merck & Co Inc - Senior Vice President, Chief Marketing Officer - Human Health*

Wet AMD? Very much.

Umer Raffat - *Evercore Inc - Equity Analyst*

So that's with the Tiespectus only, not with the first --

Eliav Barr - *Merck & Co Inc - Senior Vice President, Head of Global Clinical Development and Chief Medical Officer*

We're doing the two.

Umer Raffat - *Evercore Inc - Equity Analyst*

Oh, is that right?

Eliav Barr - *Merck & Co Inc - Senior Vice President, Head of Global Clinical Development and Chief Medical Officer*

Yeah.

Umer Raffat - *Evercore Inc - Equity Analyst*

So what's going to happen with the VEGF injection there then on AMD? Will that be concurrent? Or how is that going to --

Eliav Barr - *Merck & Co Inc - Senior Vice President, Head of Global Clinical Development and Chief Medical Officer*

No. So the way -- so DME is a good deriskingbecause it's a slower progressive disease. The data look good, then we'll go on to AMD.

Umer Raffat - *Evercore Inc - Equity Analyst*

Okay. So AMD study is still monotherapy.

Eliav Barr - *Merck & Co Inc - Senior Vice President, Head of Global Clinical Development and Chief Medical Officer*

With Wnt, yes. And the VEGF Tie2 is it's -- it should be -- that's going to be the first indication.

Chirfi Guindo - *Merck & Co Inc - Senior Vice President, Chief Marketing Officer - Human Health*

And it's a large category, as you know, Umer. So we are going to study both assets in both indications.

Umer Raffat - *Evercore Inc - Equity Analyst*

Is there a very high interest from the retina community on a new mechanism? Are you hearing that?

Chirfi Guindo - *Merck & Co Inc - Senior Vice President, Chief Marketing Officer - Human Health*

Absolutely.

Eliav Barr - *Merck & Co Inc - Senior Vice President, Head of Global Clinical Development and Chief Medical Officer*

There's a -- look, the VEGF is really important, and it's worked very well, but there's a lot of people who are failing.

Chirfi Guindo - *Merck & Co Inc - Senior Vice President, Chief Marketing Officer - Human Health*

I mean 40% is a big number, right?

Umer Raffat - *Evercore Inc - Equity Analyst*

Okay. So the first commercial positioning is VEGF failures for the launch in DME, and then you perhaps pursue that in AMD -- even though that's not what the trial is --

Eliav Barr - *Merck & Co Inc - Senior Vice President, Head of Global Clinical Development and Chief Medical Officer*

I think that it makes sense if I were a doctor.

Peter Dannenbaum - *Merck & Co Inc - Senior Vice President, Investor Relations*

And Umer, I was just going to add, thank you for asking about ophthalmology. We've called it out as one of the areas in our pipeline that is underappreciated along with HIV and just the overall breadth and depth of the pipeline, including oncology. But we've gotten a little bit more attention on ophthalmology recently, but it's a good discussion to have.

Umer Raffat - *Evercore Inc - Equity Analyst*

Got it. So again, late next year, I think you said for the readout of the Phase III.

Peter Dannenbaum - *Merck & Co Inc - Senior Vice President, Investor Relations*

Yeah. September, I think, '26 is the primary completion date. And the Tiespectus Phase II is April of '26.

Umer Raffat - *Evercore Inc - Equity Analyst*

Outstanding. Okay, great. Maybe just you happen to mention HIV. I want to move on to immunology in just a second. But on HIV, the monthly prep obviously looks -- the idea of a pill once monthly for PrEP looks very interesting. But I have noticed at least sort of going through the prior presentation, there were a couple of cases of CD4 drops, which I wonder if that was the Cmax issue. Could you speak to that?

Eliav Barr - *Merck & Co Inc - Senior Vice President, Head of Global Clinical Development and Chief Medical Officer*

Yeah, it's not a Cmax issue. I mean this was drops within the -- within very tight criteria that FDA asked us to use. There was no clinically significant issues. The FDA has kind of allowed us to move forward now. So yes, there were -- what happens is that you have these people who come up with way high CD4 counts, and that's -- they're probably -- you just measure them in some -- I don't know, for some reason. And then it goes down from top end of normal to normal.

Umer Raffat - *Evercore Inc - Equity Analyst*

Got it. Okay. Makes a lot of sense.

Eliav Barr - *Merck & Co Inc - Senior Vice President, Head of Global Clinical Development and Chief Medical Officer*

But no, there were no clinically meaningful --

Chirfi Guindo - *Merck & Co Inc - Senior Vice President, Chief Marketing Officer - Human Health*

Umer, on that note, I think the excitement around our HIV pipeline is really the opportunity to establish a new anchor treatment with islatravir, which is really a first in a new class of NRTTIs. For years, the field has been looking for one because, right now, it's integrase that is the anchor, right, of treatment.

And so as patients get older, you get concerned about long-term effects, especially cardiometabolic issues associated with integrase inhibitors. And so finally, now there is the potential to have a new anchor around islatravir for both treatment as well as PrEP, to your question. So really, really exciting.

Umer Raffat - *Evercore Inc - Equity Analyst*

Right. But Chirfi, I guess this is one molecule I've always had some amount of confusion on. Because of that legacy Gilead trial where islatravir was probably driving some of the CD4 drop problems. I think you guys lowered the dose since then. But wouldn't some of those legacy issues carry over commercially? Like how would clinicians perceive that?

Chirfi Guindo - *Merck & Co Inc - Senior Vice President, Chief Marketing Officer - Human Health*

So we've -- I mean the data is so clean. I mean you've seen that this is the switch data. And then we've announced the naive data just in the past week or two. Let's wait and see what the label says at the end of the day, but we're confident that the profile is going to be a very, very compelling one.

Umer Raffat - *Evercore Inc - Equity Analyst*

Right. Would you remind us, Eliav, what was the dose when the Gilead combo was being studied, what's the dose now?

Eliav Barr - *Merck & Co Inc - Senior Vice President, Head of Global Clinical Development and Chief Medical Officer*

Well, so we -- it was 0.75 Q-day and 20 milligrams Q week. And now we're at 0.25 Q day. We're not doing a Q week for islatravir -- I mean -- sorry, Q week for islatravir is 2 milligrams, and then it was 60 milligrams for Q month islatravir, but we're using 8527. So Q day was 0.75 down to 0.25, Q week was 20 down to 2. The problem was ---

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Umer Raffat - *Evercore Inc - Equity Analyst*

So the 20 down to 2 is really where you brought the Cmax way down.

Eliav Barr - *Merck & Co Inc - Senior Vice President, Head of Global Clinical Development and Chief Medical Officer*

Yeah. I mean the issue was -- so the issue was we wanted to have something that was so very super forgiving that you could like forget for a couple of weeks and be covered. We were a little picky.

Umer Raffat - *Evercore Inc - Equity Analyst*

Okay. Got it. So okay. Now I do want to be clear though, on 8527, which is sort of the mainstay for a lot of the future combinations as well, there is a grade 4 -- sorry, there's a grade 1 CD4 drop, but you're saying the thresholds are not as clean?

Eliav Barr - *Merck & Co Inc - Senior Vice President, Head of Global Clinical Development and Chief Medical Officer*

I mean -- yes. No, it's fine. It's going to be -- the reduction is -- this was a reduction and then it went back up afterwards. So I mean, it's -- these patients -- none of this is worrisome to us, wasn't worrisome to FDA. Didn't have any issues for the community. But look, we'll see what Phase III --

Chirfi Guindo - *Merck & Co Inc - Senior Vice President, Chief Marketing Officer - Human Health*

Umer, you said that 8527 is the mainstay of the future combinations. I don't know what you mean by that.

Umer Raffat - *Evercore Inc - Equity Analyst*

Sorry. No, sorry, I was (multiple speakers) for PrEP -- for PrEP.

Chirfi Guindo - *Merck & Co Inc - Senior Vice President, Chief Marketing Officer - Human Health*

Islatravir is the foundational for the combinations.

Eliav Barr - *Merck & Co Inc - Senior Vice President, Head of Global Clinical Development and Chief Medical Officer*

Again, as I mentioned, the grade 1 results were, as I said, minor. And again, it went back up after -- in the next measurement.

Umer Raffat - *Evercore Inc - Equity Analyst*

Got it. Okay. So let's transition to immunology. And I guess my first question is really -- and this is not because there's J&J in the audience. But my question really is there's a perception that Merck doesn't have the type of commercial infrastructure from a rebates perspective in immunology that J&J, AbbVie, Sanofi have. And does that curtail Merck's ability to launch TL1A and or continue to build it out?

Chirfi Guindo - *Merck & Co Inc - Senior Vice President, Chief Marketing Officer - Human Health*

Well, this is a new MOA, right? So one thing that we know about the space, and we learned a lot from J&J from our collaboration in Europe over many years. I was head of the Netherlands for a number of years for Merck, or MSD as it's called there, where we have the J&J collaboration with REMICADE, SIMPONI and did a great job there. It was the number one drug in the industry at that stage for a number of years. So we've learned a lot through that collaboration.

But coming back to the US, we believe the opportunity to bring a first in a new class of TL1A that has both anti-inflammatory and antifibrotic benefit will be very, very meaningful, especially in IBD where you have a recycling of patients typically, right, through MOA after MOA. And a number of patients, a great number of patients never achieve remission. So they do need this new approach.

And so we think that the commercial case is going to be very compelling. And we're not really concerned about some of those contracting barriers that you referenced, because of the unique MOA and the benefit that this will bring to patients.

And what I will also add is we're so enthusiastic about tulisokibart that we're not limiting ourselves to IBD, right? So we have the two Phase III programs ongoing that Eliav and the team are driving. We have 4 Phase II programs, in addition, right, in rheum and derm indications. So we're thinking big around tulisokibart. So this is why we've announced $5 billion-plus. I should have mentioned also in the case of HIV, $5

billion-plus opportunity. So there's a series of $5 billion-plus commercial opportunity for a number of these new categories that we're really, really excited about.

Umer Raffat - *Evercore Inc - Equity Analyst*

Got it. On the UC trial, what's the efficacy expectation, Eliav, you want to hit for that $5 billion-plus?

Eliav Barr - *Merck & Co Inc - Senior Vice President, Head of Global Clinical Development and Chief Medical Officer*

No, it has to be differentiating. Look, you have -- we have the Phase II results that showed a delta of pretty substantive

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Umer Raffat - *Evercore Inc - Equity Analyst*

Mid-twenties

Eliav Barr - *Merck & Co Inc - Senior Vice President, Head of Global Clinical Development and Chief Medical Officer*

- 26. And so I think --

Umer Raffat - *Evercore Inc - Equity Analyst*

Do you want to hit that at least?

Eliav Barr - *Merck & Co Inc - Senior Vice President, Head of Global Clinical Development and Chief Medical Officer*

We want to be able to -- the study will be successful if it will be successful. But I think being in the mid-20s would be -- would make it an important addition.

Umer Raffat - *Evercore Inc - Equity Analyst*

But placebo rates are going up, I feel in general in UC.

Eliav Barr - *Merck & Co Inc - Senior Vice President, Head of Global Clinical Development and Chief Medical Officer*

Well, I mean when you go from Phase II to Phase III, you can, I mean, there's some studies -- and this is true, by the way, across immunology. If you don't choose the right patients and you're not careful about patient selection, you end up with individuals who are -- have very mild disease and given the fact that the disease goes up and down, you have placebo rates.

We've done a really good job. One of the things -- you're right, we're new in -- we're re-entering immunology from the MRL side. But what we did is we had an on-block reception of the people that did a lot of AbbVie's drugs had moved them down to Merck. So there's a lot of --

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Umer Raffat - *Evercore Inc - Equity Analyst*

R&D or commercial?

Eliav Barr - *Merck & Co Inc - Senior Vice President, Head of Global Clinical Development and Chief Medical Officer*

R&D and commercial.

Chirfi Guindo - *Merck & Co Inc - Senior Vice President, Chief Marketing Officer - Human Health*

Yeah, we have some commercial as well. We've hired a few from J&J as well.

Umer Raffat - *Evercore Inc - Equity Analyst*

All right.

Eliav Barr - *Merck & Co Inc - Senior Vice President, Head of Global Clinical Development and Chief Medical Officer*

We basically have an AbbVie UC crew that is on the show for us.

Umer Raffat - *Evercore Inc - Equity Analyst*

And on the non-UC indication, what's your expectation on the HS trial? I believe that's next year. Should we comp it versus what a TNF does? Or should we really comp it versus the real bar with IL-17?

Eliav Barr - *Merck & Co Inc - Senior Vice President, Head of Global Clinical Development and Chief Medical Officer*

You have to do it against IL-17. Do it against IL-17. I mean that's the new standard. You can't do something if --

Umer Raffat - *Evercore Inc - Equity Analyst*

Does Merck have any visibility on either the HS trial or the SSC-ILD trial as of right now on the TL1A?

Eliav Barr - *Merck & Co Inc - Senior Vice President, Head of Global Clinical Development and Chief Medical Officer*

It's blinded, so no.

Umer Raffat - *Evercore Inc - Equity Analyst*

Blinded. Yeah.

Eliav Barr - *Merck & Co Inc - Senior Vice President, Head of Global Clinical Development and Chief Medical Officer*

Time will tell.

Umer Raffat - *Evercore Inc - Equity Analyst*

Okay. Excellent. Excellent. And which brings me to the last point. A lot of the other immunology players are very quickly moving to combinations now going forward. Because Merck is focusing on sort of new mechanism, I guess, how do you balance that from a combination perspective? Do you need partners? How does the immunology build-out look like?

Eliav Barr - *Merck & Co Inc - Senior Vice President, Head of Global Clinical Development and Chief Medical Officer*

Yeah. So we do think combinations are going to have to be done rationally. And here, I think harkening back to the oncology experiences, getting the right combination is important. One of the things, TL1A, because it's a new MOA is to understand the Phase III results and be able to build on that basis. So we're interested in combinations. There are generic drugs that are available out there, maybe partnerships that we do. We also have drugs in our Phase I pipeline that may be of interest. And so --

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Umer Raffat - *Evercore Inc - Equity Analyst*

Monospecific drugs?

Eliav Barr - *Merck & Co Inc - Senior Vice President, Head of Global Clinical Development and Chief Medical Officer*

Yeah. Yeah. And we'll be able to think about combinations and see how that goes.

Umer Raffat - *Evercore Inc - Equity Analyst*

Did you think about bispecifics? There's a lot of Chinese bispecifics available, for example, in Merck's active in BD in China.

Eliav Barr - *Merck & Co Inc - Senior Vice President, Head of Global Clinical Development and Chief Medical Officer*

Sure. I mean I think you can look at that. I mean again, the one thing that I -- so this is not an immunology specific thing. I'm just -- this is how I -- some of my concerns about bispecifics as a general principle is that there may be great on efficacy. But you have an AE event that is related to one of the arms, and you can't just chop it off and say, oh, we're going to stop that arm. You either stop the whole thing or you live with the AE.

So we have to be careful about that. It's easier to develop because it's a single product, you don't have to do contribution of components. But at the same time, it reduces your degrees of freedom to pull back if you have a problem that's related to a particular MOA. That said, we always look at we have a very active BD arm in China, and if there's something interesting --

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Umer Raffat - *Evercore Inc - Equity Analyst*

Got it. I guess, Eliav, from your seat, what's the overall conversation like with Rob and the rest of the team internally on whether enough exists now to manage through KEYTRUDA or more still needs to be done?

Eliav Barr - *Merck & Co Inc - Senior Vice President, Head of Global Clinical Development and Chief Medical Officer*

I think, look, from my point of view, we're always looking for good science and for good data and good products. Our perspective is longer term than what's been two, three, four years, five years from now. I've been at Merck for 30 years, so my horizon is a little longer than others. I want to be -- I want the next -- I want to -- when I go to Happy Acres retirement park here in Florida, my hope is that I will have left Merck in a good position for the next 30 years.

Peter Dannenbaum - *Merck & Co Inc - Senior Vice President, Investor Relations*

On that point, Rob has been clear that even post the Cidara acquisition, we're still on the hunt for great science to bolster the pipeline and bolster the long-term commercial opportunity we think we can achieve. I guess what's exciting is we've highlighted over $50 billion of commercial opportunity by the mid-30s from the existing pipeline.

We've only added to that this year with Verona and now with Cidara, and the pipeline is advancing, and we're starting to see a lot of derisking events. And 2026 sets up in a very exciting way. You talked about immunology, we have a readout in ulcerative colitis late next year.

You talked about ophthalmology readout in September. And then back to islatravir in HIV, the islatravir, lenacapavir once-weekly treatment trials readout early in the year. So it's -- everything is starting to derisk and there's a lot more visibility to this opportunity we've been talking about now for a couple of years.

Umer Raffat - *Evercore Inc - Equity Analyst*

Peter, remind us again, KEYTRUDA LOE, what are you guys -- what's the latest you guys are seeing?

Peter Dannenbaum - *Merck & Co Inc - Senior Vice President, Investor Relations*

Yeah. So the composition of matter patent for KEYTRUDA will expire towards the end December 2028. There are a couple of additional patents we've identified, it's in our 10-K, that extend out to I believe it's May and November of 2029. One is a manufacturing patent, one is a method of use patent in oncology, which we will defend and we'll have to see how that -- what the outcome of that is. But the potential is it could extend into -- well into 2029.

Umer Raffat - *Evercore Inc - Equity Analyst*

Got it. And Chirfi, from your perspective, any switch over to KEYTRUDA subcu? Does that sort of dampen the slope down, or not necessarily?

Chirfi Guindo - *Merck & Co Inc - Senior Vice President, Chief Marketing Officer - Human Health*

Well, what I can tell you is that the feedback so far is very positive for QLEX, right? And it's still early days in the US and we just received the approval in Europe last week for subcu KEYTRUDA. And so we are confirming what we have said, which is that over a period of 18 to 24 months, you're looking at a 30% to 40% adoption rate of QLEX.

And this is a -- this is an injection that you administer in less than a minute, right, for the Q3 week dose, and less than two minutes for six-week dose. It's really, really convenient for both patients. But also it helps really the institutions manage their flow and their resources got it.

So we are really excited about the opportunity to provide that value. And then we will be competitive, right? So we intend to -- we've priced it at parity with KEYTRUDA IV, as you know. And beyond the LOE period, we do intend to compete and make sure that we maintain broad access to QLEX.

Peter Dannenbaum - *Merck & Co Inc - Senior Vice President, Investor Relations*

Yeah. And the LOE on QLEX extends out to 2039. So we have a long period of time where we can have exclusivity.

Umer Raffat - *Evercore Inc - Equity Analyst*

Got it. Excellent. Maybe just in the last few seconds. Number one, Verona, without a DPI, do you think it's still competitive? And then also GARDASIL single dose, do you expect any impact from --

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Chirfi Guindo - *Merck & Co Inc - Senior Vice President, Chief Marketing Officer - Human Health*

Who knows?

Eliav Barr - *Merck & Co Inc - Senior Vice President, Head of Global Clinical Development and Chief Medical Officer*

Yes. Well, we've been clear that FDA -- today's FDA has made it clear that the current evidentiary standards are insufficient for label change. What happens with ACIP depends on ACIP, but I think they have other fish to fry at this --

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Umer Raffat - *Evercore Inc - Equity Analyst*

I think we can do another 50 minutes on today's FDA. We should leave it right there.

Eliav Barr - *Merck & Co Inc - Senior Vice President, Head of Global Clinical Development and Chief Medical Officer*

Thank you so much.

Umer Raffat - *Evercore Inc - Equity Analyst*

Thank you, guys, so much.
