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CORPORATE PARTICIPANTS

Eliav Barr *Merck & Co., Inc. - Chief Medical Officer & Head of Global Clinical Development of Merck Research Laboratories*

Peter Dannenbaum *Merck & Co., Inc. - VP of IR*

CONFERENCE CALL PARTICIPANTS

Umer Raffat *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

PRESENTATION

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

Listen, thank you guys for being here. Apologies, I'm a couple of minutes behind. Pleasure to have Merck management join us. This is our last fireside of this conference, at least from my end. So really looking forward to it. Peter promised it will be action-packed. And so let's jump right into it.

QUESTIONS AND ANSWERS

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

I think it will be a great idea, maybe let me turn it over to you, Peter and Eliav, to kick things off. Maybe frame for us what's on top in terms of priority list on your mind, and we'll jump right in.

Eliav Barr - *Merck & Co., Inc. - Chief Medical Officer & Head of Global Clinical Development of Merck Research Laboratories*

Sure. This has been a tremendous year for Merck, and we're looking forward to 2024. The things that are top of mind for us, continued news on KEYTRUDA, especially in early-stage cancers. The -- you're going to see a large number of Phase III starts for all of our antibody-drug conjugates that we have partnered with Kelun and with Daiichi Sankyo, a large number of efforts in precision medicine in oncology as well as, of course, V116, the filing, and then, hopefully, if all goes well, the approval of that.

Sotatercept is -- should be entering the commercial space, and we're looking forward to seeing that. There may be additional data coming from the ongoing studies that are event-driven like the ZENITH study. And as we've talked about before, our oral PCSK9, MK-0616, has started Phase III programs, including our cardiovascular outcome trial.

We have Phase III start for MK-7240, formerly PRA023, our TL1A antagonist. And then, of course, continued work on MK-060 which is our compound for NASH. And it has some weight loss benefits as well. So a lot going on, a very diversified pipeline, a very busy year going forward.

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

Excellent. I know you mentioned KEYTRUDA, and I want to go through each of those. But maybe just before we get into more product-specific stuff, Peter, can I just start by asking? I know there was a fair amount of confusion on it a few weeks ago around the margin profile, what Merck is saying, whether the commitment to the margin target stays fully intact. Could you just remind us on that?

Peter Dannenbaum - *Merck & Co., Inc. - VP of IR*

Yes. No. Thank you, Umer. So from a margin standpoint, we continue to point to the achievement of additional margin expansion. We've been on quite a record of margin expansion over the last several years, including in 2023. We expect further margin expansion in 2024, driven by product mix. So as KEYTRUDA and GARDASIL continue to grow strongly, as we expect, that's a benefit.

And we also have the roll-off of some significant royalties both for KEYTRUDA and GARDASIL. KEYTRUDA rolls down from 6.5% to 2.5% and -- on global sales. And GARDASIL, there's a royalty that we paid at Glaxo that is now 7% that will roll down to 0. So we'll benefit from that.

And we will continue to tightly manage SG&A, but making sure we invest in our growth drivers. R&D, we will continue to invest. And we've expanded our pipeline pretty dramatically, so we'll continue to ensure that we fund those programs. So you'll see R&D continuing to increase.

As we look out to 2025, we have had a target for 43%-plus operating margins, and we continue to believe we'll achieve that. What Caroline has said, to the degree the pipeline continues to expand, we're not going to forgo necessary investments that would fully optimize those pipeline assets and lead to better long-term growth. But right now, as we stand, 43%-plus is something that we would continue to point to.

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

Okay. Excellent. That's very helpful. And maybe just one more as a quick follow-up on that. I know there's KEYTRUDA growth, a fair amount of growth still modeled in. I think, Eliav, you mentioned about some of the additional indications coming online. There's underlying momentum and next year's launch is ongoing as well.

If I look at consensus numbers, KEYTRUDA has been modeled in from -- in going from about $25 billion to perhaps $35 billion over the next 5 years or so. I know you guys have clearly expressed enthusiasm on the momentum continuing. Could you just expand on expectations of KEYTRUDA? Because that's critical to some of the margin expansion as well, obviously.

Peter Dannenbaum - *Merck & Co., Inc. - VP of IR*

Yes. So I'll start from a commercial standpoint. Eliav, if you have anything to add from a clinical perspective, feel free to. But we continue to expect strong growth of KEYTRUDA, and we don't give product-level guidance typically. But as I just suggested in your prior question, we do think that 2024 will be another year of strong growth for KEYTRUDA, albeit -- I mean we've had exceptional growth for KEYTRUDA over the last year or 2 years. And the third quarter annualized run rate was $24 billion-plus. So the types of percentage increases that we've seen in the last year or 2 are -- would be difficult to achieve. But I think consensus has already reflected that as they've modeled out 2024, and we think that's appropriate.

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

Right. I think the point that was made previously was don't expect 20%-plus type of growth going forward. But conversely, wouldn't EV-302 just create a very significant tailwind into next year, especially given the first line, especially given the duration that we saw? There's a -- it seems to me that there's a realistic chance KEYTRUDA just vastly outperforms numbers into next year. It could actually approach meaningfully north of the types of 10% kind of numbers.

Eliav Barr - *Merck & Co., Inc. - Chief Medical Officer & Head of Global Clinical Development of Merck Research Laboratories*

Well, it's a great -- the results are -- speak for themselves. I think it's outstanding results. And so we really look forward to having those data come through. And I think everyone we've talked to, including the regulators, are very excited about the results. So I think that's really great.

And KEYNOTE-671, KEYNOTE-564, those are 2 other ones that I think are really important. For the first time, there's overall survival benefit for interventions in the perioperative stage -- state, and they're both with KEYTRUDA and they're both only KEYTRUDA. No other of the IO compounds have been there. So I think that there's some really exciting momentum from that. It's the -- tell me about the commercial stuff.

Peter Dannenbaum - *Merck & Co., Inc. - VP of IR*

I mean, I think we are excited by KEYTRUDA's move into earlier-stage cancers, as Eliav suggests. So there's a lot of opportunity for continued growth. We've pointed to early stage representing over half of KEYTRUDA's growth as we look out to 2025 and to represent 25% of global KEYTRUDA sales in that year. So the early stage is important. Certainly, bladder, lung will become increasingly important as well, some of the women's cancers that Eliav mentioned as well. So continue to be very confident with the growth of KEYTRUDA.

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

Got it. Makes sense. As I start to transition to pipeline, I thought maybe since we were talking KEYTRUDA, let's start with the oncology pipeline. There's broad buckets. I think of it as IO-IO, where we could have new IO modalities, including the PCV, including TIGIT. We could have ADCs and then some small molecule efforts, unless I missed any other major chunk.

Eliav Barr - *Merck & Co., Inc. - Chief Medical Officer & Head of Global Clinical Development of Merck Research Laboratories*

That's pretty good.

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

So on the IO-IO side, Peter would always tell you, TIGIT's always on top of my mind. Is the Moderna cancer vaccine on top of Merck's mind?

Eliav Barr - *Merck & Co., Inc. - Chief Medical Officer & Head of Global Clinical Development of Merck Research Laboratories*

Every -- look, we have a broad portfolio. Each one of these is exciting, and we've spent -- we've invested quite a bit in it. The INT or V940, I think, is a really big opportunity because it's very unique and it's got the ability for durable long-term drug-free effects. So like every immunotherapy of its sort, the expectation here is that there'll be benefits even after the medicine -- the medical therapy is done. And we'll see how that goes. There's going to be further cuts of the data going forward for the study -- the Phase II study in melanoma.

You've seen the melanoma Phase III program start. We're going to have a heavy jump into lung coming up, and there'll be several other studies that will initiate in 2024. We have done a really nice job. Moderna has done a really nice job in building the capacity ready for clinical trials. So that's really great.

TIGIT, there will be a presentation of KeyVibe-002 in about a week at the ESMO IO conference, which data is still embargoed until about 6 tonight. And then you'll be able to see what we -- what all the hoopla was about. So that will be exciting. And then, of course, the first-line lung and the adjuvant melanoma program continue at pace. It's just they're big studies, and they require both enrollment and follow-up. So...

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

Adjuvant melanoma. Are you talking about the PCV or...

Eliav Barr - *Merck & Co., Inc. - Chief Medical Officer & Head of Global Clinical Development of Merck Research Laboratories*

Both. KeyVibe-010.

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

KeyVibe-010. Oh, so you're talking about TIGIT?

Eliav Barr - *Merck & Co., Inc. - Chief Medical Officer & Head of Global Clinical Development of Merck Research Laboratories*

Yes. So yes, the -- so with the PCV, with the INT compound, we -- Phase III starts. Phase II should be in 2024. For TIGIT, KeyVibe-002 will be presented in a week. The abstract should be viewable later on today. And the Phase III program continues and will -- it's just a matter of now enrollment and time. Critical completion dates are later -- are not next year but the year to follow. But there's interim analysis, and we'll have to see how that goes.

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

Got it. Okay. Anything notable on the KeyVibe-002 we should keep in mind? It was a trial of triplet versus -- triplet, PD-1, chemo, TIGIT versus just PD-1 -- sorry, versus just PD-1 plus TIGIT versus chemo. We know the doublet was dropped. We know the triplet was moved forward. Data is tonight. You said exciting data. But also, this is not a first-line trial, which is...

Eliav Barr - *Merck & Co., Inc. - Chief Medical Officer & Head of Global Clinical Development of Merck Research Laboratories*

It's not.

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

Anything else notable we should just know about the trial design?

Eliav Barr - *Merck & Co., Inc. - Chief Medical Officer & Head of Global Clinical Development of Merck Research Laboratories*

Well, I think that the key there is to ask the question about -- to try to figure out, are there ways to gain really -- looks at whether TIGIT added to a strong PD-1 has benefits. And there's been -- this study doesn't directly look at that because there's no pembro-only arm. But at the same time, these are people who are all been experienced with -- who have had PD-1s and we know what their objective response rates, which are usually single digit to the very low teens.

And so I think it provides a piece of data we've seen with the TIGIT compounds, however, and we have to acknowledge that there have been Phase II studies that have looked good. And then there's been Phase IIIs that have been more complex. And so my -- the way I see the compound is we would wait to see for Phase III and go from there.

We have a very robust program across the lung space, which is where we think this might be useful in melanoma. So I think that's -- those 2 sets of tumors are really important and have the best opportunity for showing incremental value that's of sufficient size to be meaningful for patients.

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

Makes sense. Eliav, also I think the other aspect of this TIGIT trial which is particularly relevant is so, A, you mentioned these are PD-1-experienced patients. The other dynamic is they're not selective for PD-L1 highs or lows. These are all-comers. Should we -- again, there's prior data from Roche

focusing on PD-L1 super highs only. There's other data sets suggesting the benefit did continue. There's no reason why a TIGIT should work only in PD-L1 highs or not?

Eliav Barr - *Merck & Co., Inc. - Chief Medical Officer & Head of Global Clinical Development of Merck Research Laboratories*

No. I think be careful about the post-hoc analysis. I don't know what to make of -- in small data sets as well. If you look at what we're doing in our clinical trials program, we are essentially following the paradigm of where pembro has been approved. So pembro is approved as monotherapy in people with TPS greater than 1%, PD-L1 as monotherapy. And so we have a trial of TIGIT plus pembro against pembro. The study is large enough to look at the greater than 1% and greater than 50% separately.

We have a study of pembro, TIGIT with chemo versus pembro with chemo. So the standard regimen against a standard regimen plus pembro in first-line non-small cell lung cancer. We've got a Stage 3 study, KeyVibe-006. And then we've got studies in small cell. So we'll see how that goes. And then again, KeyVibe-010 is a study in adjuvant melanoma in patients with Stage 2 and 3. Each of those studies is -- every one of these studies is characterized by the fact that pembro is foundational for that tumor. And that's the -- and so we're just adding TIGIT on top of that.

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

Got it. One last, KeyVibe-002, primary endpoint was PFS, not ORR. And we should expect at the ESMO IO presentation book that we're...

Eliav Barr - *Merck & Co., Inc. - Chief Medical Officer & Head of Global Clinical Development of Merck Research Laboratories*

To have everything.

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

Have everything?

Eliav Barr - *Merck & Co., Inc. - Chief Medical Officer & Head of Global Clinical Development of Merck Research Laboratories*

Yes. With some OS data.

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

Okay. Got it. Excellent. Maybe perhaps, starting to move on, on the Merck -- sorry, on the Moderna PCV program, V940. One of the questions -- and I remember having some discussion with Peter on this too. There's a presentation at ESMO which dug into data breakdown by BRAF mutation. BRAF mutants are not wild type. And then further by, I forget now, it was the cTDNA status. And it looked like the benefit was coming from one of the 2 subgroups. And even within that subgroup in cTDNA negatives, I was just thinking out loud about how should we think about that because there's been always questions around how robust is the signal. It looks very good overall. But then the fact that it's driven by one subgroup and not totality makes you wonder, could it be a false positive for you?

Eliav Barr - *Merck & Co., Inc. - Chief Medical Officer & Head of Global Clinical Development of Merck Research Laboratories*

No, I don't think so because I think we have -- like everything in the small Phase II studies, confidence intervals are very large. And then there's things that are -- that favor the...

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

You mean baseline?

Eliav Barr - *Merck & Co., Inc. - Chief Medical Officer & Head of Global Clinical Development of Merck Research Laboratories*

Yes, the baseline things that are favoring the...

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

In the subgroups?

Eliav Barr - *Merck & Co., Inc. - Chief Medical Officer & Head of Global Clinical Development of Merck Research Laboratories*

Among all the different parameters that might impact presence of cTDNA, different PD-L1 status, whatever, all of these different things, there is imbalance between the groups, as you would expect in a Phase II study that's so small. But things that -- a priority, you'd think, would favor control versus favoring the combo, pretty much evenly distributed. It's really hard to tell.

But it's fair to say Phase III is where we prove efficacy. And we're very excited about this. Obviously, we've invested quite a bit, not just in clinical trials but also in the setup for manufacturing. And we think that notwithstanding some baseline imbalances that go -- that favor one arm or the other, that the overall picture is one that's very promising indeed.

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

Got it. Maybe -- okay. Anything else on IO-IO before we transition on?

Eliav Barr - *Merck & Co., Inc. - Chief Medical Officer & Head of Global Clinical Development of Merck Research Laboratories*

No, that's it. Yes.

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

Okay. On...

Eliav Barr - *Merck & Co., Inc. - Chief Medical Officer & Head of Global Clinical Development of Merck Research Laboratories*

ADCs?

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

Perhaps ADCs because there are several things to go through there. Obviously, there's the collaboration that was announced with Daiichi recently. One of the questions that came up was what was the primary basis of that deal? There were 3 programs that came in. My understanding is it was the -- perhaps the B7-H3, which was really the impetus behind it. I don't know to what extent that's true, realizing that HER3 was more further along.

Eliav Barr - *Merck & Co., Inc. - Chief Medical Officer & Head of Global Clinical Development of Merck Research Laboratories*

Well, I think each one of these assets is really exciting. And I think Caroline had said that she hopes that we have all the -- we'd pay all the milestones so that we -- so that -- because that would mean the best benefit for patients, everything will work out great.

So B7-H3 is exciting because of the small cell and some potential in prostate. And there are other things. Obviously, we're just at the beginning of the investigation for that. We really -- I really like the HER3 ADC because I think that it has opportunities to both -- to be active in various forms of driver lung cancer sort of settings. And here, I mean things -- we know the EGFR mutant, but we're also looking at other driver mutations like KRAS and also interested in other cancers. So I think that there's a really nice opportunity with patritumab that we're really looking at. And during the due diligence, we were really excited about that as well.

CDH6, I think, is topical because of today's news about the ImmunoGen acquisition by AbbVie because it's about ovarian cancer present. The early data as presented look very, very promising indeed. It's Phase I., so we're just beginning the investigation there. But I do think that we have a strong history in ovarian cancer and a really great basis for -- and a set of trials that I think will serve us well to help position CDH6 as an essential medicine in that treatment.

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

So maybe working off of that CDH6 ADC, I realize the efficacy was clearly very intriguing. It also is clear that a couple of higher doses were dropped because of therapeutic index reasons. Do you think at doses that are realistically possible for an extended interval dosing, we have the right therapeutic index and we have encouraging efficacy at those doses which are realistic?

Eliav Barr - *Merck & Co., Inc. - Chief Medical Officer & Head of Global Clinical Development of Merck Research Laboratories*

Yes, because the dosing starts -- or the activity starts at 4.8 MPK. And we're going, I think, 5.6 and 6.3, I think, as there's 3 arms. And one of the things that has been very useful in our collaboration is that our colleagues in Daiichi have learned a lot about the therapeutic index and dose selection based on their first 2 ADCs. And I think that they're much more sophisticated in the modeling and the approach to choosing the sweet spot for the next 3. And I think we're not going to have the kind of ILD issues that we see.

Of course, at higher doses with all of these drugs, you will reach a point where there's toxicity. But what's interesting about CDH6, just as an example, is that the activity well below the ILD doses is pretty exceptional. So we're thrilled about this. It's -- and by the way, the activity was in an unselected population. Don't need to know about folate receptor alpha status. So I think it's going to be a very key part of future therapies for ovarian cancer.

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

Got it. HER3 ADC, this was being filed in EGFR mutant lung cancer.

Eliav Barr - *Merck & Co., Inc. - Chief Medical Officer & Head of Global Clinical Development of Merck Research Laboratories*

Correct.

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

If you and I spoke a few months ago, I would have said, oh, your TROP2 ADCs is going into that indication. I guess, how are you guys thinking about that? Or do you intend to have 2 different programs for EGFR mutants?

Eliav Barr - *Merck & Co., Inc. - Chief Medical Officer & Head of Global Clinical Development of Merck Research Laboratories*

Yes, I think we will. I think that there's -- while for the most part, the 6 ADCs are unique in their own areas, there are a couple of areas of overlap. I think it's okay because there's enormous opportunity for -- in the space because we already see that once patients fail successive rounds of EGFR inhibitors, the cancers are really -- they have very, very short time to demise. And so I think that there's a lot of opportunities there both in terms of looking at TROP levels or HER3 levels or looking at sequencing the ADC. So I actually don't think that that's going to be an issue. Both agents are very active. And I think we'll be able to provide options for people with somewhat different AE profile. So we'll see. Both of them are going to go forward.

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

Got it. So I realize the TROP2 ADC, which you guys got from the Chinese partner, Kelun, as well as your -- some of the newer stuff that you got from Daiichi, including the HER3, they're both topoisomerase-based payloads. But within that, you could have differences in potency on the exact type of payload. So my understanding is Daiichi is exatecan, which is less potent, much less potent than irinotecan. Can you remind me, is the Kelun TROP2 irinotecan?

Eliav Barr - *Merck & Co., Inc. - Chief Medical Officer & Head of Global Clinical Development of Merck Research Laboratories*

No, it's a derivative of belotecan. So again -- and you have different DARs, and so there -- it's all -- it's very hard to do cross-comparisons. But I can tell you, 2870 again has been exceptionally active for us. We're really excited about it as well. We've seen 2 clinical studies already entering clinicaltrials.gov in Phase III. They've already started. We've started enrollment. And then next year, there should be a pretty substantive number of trials for 2870 moving forward.

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

Got it. Excellent. Anything we missed on ADC just before we move on?

Eliav Barr - *Merck & Co., Inc. - Chief Medical Officer & Head of Global Clinical Development of Merck Research Laboratories*

No, I think -- MK-1200, our Claudin-18.2 ADC is moving along very quickly. And again, that's a unique profile. That will be exciting as well.

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

Got it. One minor question I forgot and I just got an e-mail about it. On TIGIT, a couple of your competitors have talked about how Merck has lowered the dose. What's the back story there? I meant to ask that.

Eliav Barr - *Merck & Co., Inc. - Chief Medical Officer & Head of Global Clinical Development of Merck Research Laboratories*

There isn't. There's no back story. I mean we never reached MTD, so we went all the way up to 700 milligrams. There's no reason to have it. And we know there's complete saturation of the receptor based on our modeling at 200. There wasn't a safety issue. We just reached kind of the plateau. There's no reason to go higher than full saturation.

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

Okay. So all the trials are using 200 now going forward?

Eliav Barr - *Merck & Co., Inc. - Chief Medical Officer & Head of Global Clinical Development of Merck Research Laboratories*

It is, yes.

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

And the one that's being reported in lung right now, [the 2.0s], they're all 200?

Eliav Barr - *Merck & Co., Inc. - Chief Medical Officer & Head of Global Clinical Development of Merck Research Laboratories*

200. Yes.

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

Okay. Got it. Final point on oncology, just before we graduate on small molecules. A couple of programs I had on my mind, HIF-2 and the BTK. We can discuss any of the programs you'd like. On HIF-2, where do things stand? I feel like there's a lot of interest in this. I realize the initial approval was in a more tumor -- mutation selective, so it was a much more smaller subgroup. Do you see a path now to a much broader approval? And when would that be?

Eliav Barr - *Merck & Co., Inc. - Chief Medical Officer & Head of Global Clinical Development of Merck Research Laboratories*

Yes. So LITESPARK-005, which is our first study in all-comer renal cell cancer, read out positive for PFS in the chief priority review, and we'll have a PDUFA date in first quarter next year. And I think it's a great example of how HIF-2 alpha can be an excellent anticancer drug outside of this -- the germline VHL setting.

Renal cell is going to be where the main focus of activities are because there is a lot of somatic mutations of VHL as well that is associated with carcinogenesis. So we have studies in the frontline. We have in IO failures. We have in the adjuvant setting. And this kind of builds on our -- on the enormous body of data with KEYTRUDA in the renal cell space. There's just -- we'll have offerings across the different levels of disease for clear cell and non-clear cell. And I think that's going to be very important.

We do have trials going on now with the HIF-2 alpha in patients with other kinds of mutations. Those data are cooking and may very well provide an additional area for use of this drug above and beyond renal cell. So there's a lot still going on with belzutifan where we really are first and only.

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

Got it. Peter, I see very modest growth in consensus numbers on the HIF-2, $200 million to $300 million. Has there been much discussion on this on sort of momentum into a potential broader approval next year?

Peter Dannenbaum - *Merck & Co., Inc. - VP of IR*

So among analysts and investors? Not a lot, no. So we have -- it has not received a ton of attention. We've consistently said we see strong expectations for WELIREG longer term and believe it can be a blockbuster.

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

Got it.

Eliav Barr - *Merck & Co., Inc. - Chief Medical Officer & Head of Global Clinical Development of Merck Research Laboratories*

Yes. I think it's...

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

And next year, this PDUFA opens that up is how I would think about it.

Eliav Barr - *Merck & Co., Inc. - Chief Medical Officer & Head of Global Clinical Development of Merck Research Laboratories*

Yes, I think so. Look, the VHL data were objective response rate data based on a single-arm study. So obviously, people talk to themselves. There's different people with a specific genetic defect. I think that this is a breakthrough, what we see right now, in the sense that it opens up a much broader patient population. I look at this kind of like PREVYMIS. It's a drug that is always under the radar screen, and yet it makes quite a bit of impact and therefore money.

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

Got it. Excellent. Finally, BTK, I feel like we've seen Loxo continue to be very active at ASH meetings with data updates, path to approval, et cetera. There was sort of a big ArQule data sets at Merck, went into a big quiet zone for a while. I know you guys started to come out last year. But if we do some of the data comparisons versus data being reported by Loxo, I kind of get a sense, broadly speaking, mid-50s for you guys versus anywhere from 60s to 80s for Loxo, depending on how you look at CLL, et cetera. How are you thinking about that? Is there baseline differences that explain some of those discrepancies?

Eliav Barr - *Merck & Co., Inc. - Chief Medical Officer & Head of Global Clinical Development of Merck Research Laboratories*

There are actually. I think they are different patient populations. We can talk about the cross-study comparison issue and all that good stuff. But the specific elements are they looked at and had a very large number of patients who were intolerant to BTK inhibitor -- to IBTK, to the irreversible ones. We were -- we focused all of our attention on those with C481S and related mutations. So we had more mutant patients.

The first sets of data from Loxo, they had a median prior rounds of therapy of 3. We had 4. So it's -- I don't think that there's -- that it's clear that these cross-study comparisons are like-to-like. I think it's apples-to-oranges.

As a measure of our commitment, you will have seen that we have a fairly robust Phase III study, including a study that Loxo has not done, which is our first-line study. It just popped up on ct.gov, which is called BELLWAVE-010. So I think you'll see here that we have a lot of confidence and put money behind this after -- you're right, there was a quiet zone. It was mostly we're just ensuring that we got the dose absolutely right, got that sweet spot, and took our time to do so. But I think we're in the right position now, and it's going to be an interesting next few years for the field.

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

Excellent. Maybe that might be a good point now to transition then towards some of the stuff beyond oncology. Unless there's any questions on oncology in the audience, then I'm happy to make it interactive. Okay. Sotatercept, obviously, it was a big hit in the trial that came out. STELLAR was stellar is what I call it. But I feel like amidst all the discussion on PAH, there's almost a non-PAH or a different type of PAH where nothing is approved, the Group 2 trial, which I think is a full new indication.

Eliav Barr - *Merck & Co., Inc. - Chief Medical Officer & Head of Global Clinical Development of Merck Research Laboratories*

That's right.

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

It's -- where are we with that? Could you also remind people how is that different from the standard PAH? Because it's more like a HFpEF that not.

Eliav Barr - *Merck & Co., Inc. - Chief Medical Officer & Head of Global Clinical Development of Merck Research Laboratories*

Yes. So there are different groups that WHO classifies pulmonary hypertension into different groups. PAH is the idiopathic genetic-associated specific pulmonary vascular issue. Group 2 is where we are -- what we're talking about with this trial called CADENCE. It's in patients who have both pre- and post-capillary pulmonary hypertension.

So they have heart failure usually from HFpEF and their response in pulmonary vasculature is overexuberant. It's really quite dramatic. And you have substantial increase in pulmonary arterial pressure above and beyond what you might expect due to pulmonary venous congestion.

The reason why it's taken a while to enroll that study because there's nothing for these patients, so it's not like they're warehoused or pre-identified. A lot of the work that we're doing now is actually to do the right kinds of -- right heart caths and screening patients so that we can identify the patients. This is true in a variety of diseases where there's 0 opportunity to help these patients. So you end up with having to start the screening process to bring out the patients. But once there's something that will make a difference for them, then the docs will have a reason to do the screening.

So Phase II is always for these kind of new indications where there's not much out there. Takes a while. And we'll get there. We're -- we have a PCD next year. And hopefully, the results will warrant further study.

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

Got it. Excellent. Recruiting, could you remind us how is that tracking with the [different] trial?

Eliav Barr - *Merck & Co., Inc. - Chief Medical Officer & Head of Global Clinical Development of Merck Research Laboratories*

It's been slower than we expected. But again, this goes back to this whole business of it's not like there's a whole warehouse of patients waiting for something because there hasn't been anything for them. So there's no reason for docs to pre-identify them as a patient population. So we have to go and screen for them, and that's why it's taking a little longer. But we have a lot of really great sites, and I think we have slow and steady wins the race kind of thing.

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

Okay. Excellent. Any questions in the audience?

Unidentified Analyst

(inaudible)

Eliav Barr - *Merck & Co., Inc. - Chief Medical Officer & Head of Global Clinical Development of Merck Research Laboratories*

What's up? If it was for me, at 6, okay?

Unidentified Analyst

(inaudible)

Eliav Barr - *Merck & Co., Inc. - Chief Medical Officer & Head of Global Clinical Development of Merck Research Laboratories*

Yes. And this is not -- is this PFS?

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

Yes, PFS.

Eliav Barr - *Merck & Co., Inc. - Chief Medical Officer & Head of Global Clinical Development of Merck Research Laboratories*

Okay. So the study was -- so remember, the study was a Phase II trial. We weren't really planning on looking at it from a statistical significance point of view. The poster, you'll see some interesting results on the shape of the curve and the -- and what we anticipate will be the overall view.

I think that these results, again in second line, are encouraging to us because we have -- it's not a filing study, right? And it was just designed as a signal-finding evaluation. They're encouraging for us because, again, it just shows that you -- that when you add the TIGIT to the docetaxel, you get a pretty substantially improved outcome.

And again, this is small numbers of patients, has a ratio of 0.77. It translates to a trend in OS. Good enough for us for what we were looking for to confirm the investment for the first line.

Unidentified Analyst

(inaudible)

Eliav Barr - *Merck & Co., Inc. - Chief Medical Officer & Head of Global Clinical Development of Merck Research Laboratories*

No, there's -- we're already in first line, so might as well.

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

Got it. Okay. Anything else in the audience? Can we perhaps transition then to some of the other parts of your business? I know -- so I want to talk about pneumococcal vaccines, obviously. I want to talk about the oral PCSK9 as a broader cardio strategy. Let me just hit up on a couple of questions that came in from the audience as well. One question was, can you ask about other oncology modalities like T cell engagers, cell therapies, interest in those?

Eliav Barr - *Merck & Co., Inc. - Chief Medical Officer & Head of Global Clinical Development of Merck Research Laboratories*

I don't -- where we want to go is we want to go to places where we can do the best benefit for patients and leverage the huge infrastructure that we have here. We've chosen at present not to go into cell therapy, although we have some collaborations going on. We're always looking for exciting opportunities. And so if there's some interesting T cell engagers or other modalities that we have going forward, we'll definitely...

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

Internally?

Eliav Barr - *Merck & Co., Inc. - Chief Medical Officer & Head of Global Clinical Development of Merck Research Laboratories*

I'm talking about externally.

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

Externally?

Eliav Barr - *Merck & Co., Inc. - Chief Medical Officer & Head of Global Clinical Development of Merck Research Laboratories*

Yes. So we have a collaboration with Dragonfly and TriNKET. It's an NK cell engager work. And as I mentioned and as Peter noted, we're always looking for new agents and we're modality-agnostic. We just haven't been in cell therapy because the infrastructure for that is a lot. We already have seen that in something less complex like the INT cell therapy is an order of magnitude bigger than that.

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

Okay. Another one that came in is, broadly speaking, you have an oral PCSK9. You have a GLP-1, I think, which...

Eliav Barr - *Merck & Co., Inc. - Chief Medical Officer & Head of Global Clinical Development of Merck Research Laboratories*

No, we have the NASH compound, the GLP-1 GCGR.

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

GLP-1 GCGR. It doesn't have an A1C benefit. It has a weight loss benefit?

Eliav Barr - *Merck & Co., Inc. - Chief Medical Officer & Head of Global Clinical Development of Merck Research Laboratories*

It has the most important thing. It's got a NASH benefit.

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

It's got a NASH...

Eliav Barr - *Merck & Co., Inc. - Chief Medical Officer & Head of Global Clinical Development of Merck Research Laboratories*

But that's outstanding and much more robust than semaglutide or any other drug. But it has also about 10% to 12% weight loss benefit. So it's a really good drug for NASH, and we're looking forward to evaluating it there. I think we have a whole cardiometabolic program. And I think that our focus here is NASH as the anchor around which we build other things.

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

I guess the question that comes up is, to the extent you have an injectable incretin, you have an oral PCSK9, I would have thought you might even be interested in expanding the oral PCSK9 to beyond, let's say, oral GLPs, maybe oral hypertension molecules. There's like orals in development that are novel programs. Is there any interest in going down that directions?

Eliav Barr - *Merck & Co., Inc. - Chief Medical Officer & Head of Global Clinical Development of Merck Research Laboratories*

So the macrocyclic platform that we built, I think, is really useful. And we're very interested in looking at a whole array of things where there's injectables because we really think that oral administration democratizes access. And so -- but the key has to be something that's differentiating and is valuable. We've seen that there are orals. Obviously, Rybelsus and then orforglipron is out there. If we're looking at their developments, we're thinking about second and third generation sort of things.

What are the things that are missing in the current therapies? They're amazing in terms of weight loss. It's been really beautiful to see the field grow. But we have to think about our long-term durability and tolerability. We have to think about whether the kind of weight loss that is being affected is the right kind of weight loss in the sense of muscle wasting versus fat. And so I think that there's still opportunities to improve on these. And I know that all the companies, including the...

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

Are there pockets out there which could do this without hitting muscle?

Eliav Barr - *Merck & Co., Inc. - Chief Medical Officer & Head of Global Clinical Development of Merck Research Laboratories*

There might be opportunities. I mean I think that there's a lot of -- there's -- some groups are looking at myostatin. Some people are looking at other -- a completely different mechanism of action. I think the problem with -- as you know, with muscle wasting, sort of issues with these drugs is that if people go off drug, first of all, you lose muscle, and it's not what you need when you're -- especially as you grow older.

The second piece is that when you get off therapy, then you have a real big jump up in weight because muscle is where there's a lot of energy sink in -- just in the resting state. So people are in a much more -- a much lower basal calorie use. And so you get this kind of overshoots of weight gain. So it's not such a good idea to have that if you can get around it. I think everyone is looking for that secret sweet spot. But we're -- I think the data aren't quite there yet. There's a lot of opportunities in the basic space to think about it.

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

Got it. Maybe -- I realize we're short on time, so I want to be respectful. Pneumococcal vaccine, this is the last question from my front, unless there's anything in the audience. Obviously, Merck has been able to go beyond just the PCV20 based on V116, which doesn't have a lot of the shared serotypes, et cetera. Is there a future program where Merck could deliver all the 13 shared and an additional 11? Have something in the -- well into the 20s on one vaccine, which just works in infants and in adults?

Eliav Barr - *Merck & Co., Inc. - Chief Medical Officer & Head of Global Clinical Development of Merck Research Laboratories*

Well, the reason to do that is if the biology is the same or the epidemiology is the same, and it's not. So we're perfectly comfortable as we have now with separate vaccines for babies and for adults. And so we'll continue to build the adult platform. For babies, of course, we've talked about V117 and the growth of the new -- more -- with the franchise. And we have V117, which is -- has more types that are going to be added on.

So I don't -- we're not shy about adding on to the pediatrics, but we're -- we would do that in the context of what makes sense for pediatric disease. So I'm not worried about having a vaccine that has multiple -- more types than 15, which is what we have. But it just has to be the right one. It may not be the same as V116 at all.

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

And does V117 have to be beyond PCV20 to be competitive commercially?

Eliav Barr - *Merck & Co., Inc. - Chief Medical Officer & Head of Global Clinical Development of Merck Research Laboratories*

I think it depends how the field goes because remember, there's a lot of excitement. But then you need to get the pediatric data that you need, GSK Affinivax, Sanofi has something, and I'm sure that Pfizer is going through. So we just have to see what transpires. But we're planning to go and to add more types and to do as many as we can that makes sense not just to say, oh, X is greater than X minus 1, but to really hit the important ones that cause both invasive pneumococcal disease, pneumococcal pneumonia and otitis media in babies.

But the point is that the epidemiology, the types included, have to be what's relevant for the kids. In adults, they get their own vaccine because they have different disease. That's just the way it is.

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

Excellent. Unless you have anything else, we're going to go ahead and wrap up at least my HealthCONx for 2023. All right. Thank you, guys. Thank you for joining us.

Eliav Barr - *Merck & Co., Inc. - Chief Medical Officer & Head of Global Clinical Development of Merck Research Laboratories*

Well, thanks for having us.

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

Great seeing you all.

Eliav Barr - *Merck & Co., Inc. - Chief Medical Officer & Head of Global Clinical Development of Merck Research Laboratories*

All right.

Peter Dannenbaum - *Merck & Co., Inc. - VP of IR*

Thank you.