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CORPORATE PARTICIPANTS

Roger Dansey *Merck & Co. - Senior VP, Clinical Research*

Teri Loxam *Merck & Co. - Vice President, Investor Relations*

CONFERENCE CALL PARTICIPANTS

David Maris *Wells Fargo - Analyst*

PRESENTATION

David Maris - *Wells Fargo - Analyst*

Good afternoon, everybody. I'm David Maris, Wells Fargo Specialty Pharmaceutical analyst, [kind of] large cap pharmaceutical analyst, too, although I haven't launched on the large cap pharmaceuticals yet. So, I don't know if I can officially say that, but since we are introducing a large cap pharmaceutical company, I'll take that title, too.

Very pleased to have the management from Merck here with us. Joining us from Merck, Roger Dansey, Senior Vice President, Clinical Research of Oncology, the lead clinical for KEYTRUDA and oncology, so certainly the most -- I guess I could say the most important product for Merck, but I'm sure they have several most. Teri Loxam is the Vice President of Investor Relations, also joining us in the dais.

This is a fireside chat. Since we have not launched coverage, I'm fairly limited in our questions, but I'm going to kick it off and talk a little bit about our recent meeting at Merck. But, I'm going to move on over because it's awkward if I'd ask from here. But, thank you for joining us.

QUESTIONS AND ANSWERS

David Maris - *Wells Fargo - Analyst*

So, one of the questions I have, during our meeting, Ken talked about KEYTRUDA. And at some point -- I don't know if it was Ken or someone else -- said this could be -- this isn't our guidance, this isn't -- but what if this is a $10 billion or $15 billion or $20 billion drug? And people hear numbers like $10 billion, and it's hard to fathom for an individual drug, but maybe talk about the different markets and the number of patients. And is that a number that, even though you're focused on the clinical side, that you say, well, yes, if we look at the overall market (inaudible) the patients [it's] treating, how it's treating the patients, that that's something that's achievable?

Teri Loxam - *Merck & Co. - Vice President, Investor Relations*

Why don't you start with the patient, different tumor types?

Roger Dansey - *Merck & Co. - Senior VP, Clinical Research*

Sure. I'll focus on the clinical. So, I think we're in an unusual place. We've discovered a PE-1 inhibitor, or the pathway that looks like it's genuinely relevant almost across all tumors, to some degree. And that (inaudible) [a first]. There's really not a good example in oncology of an agent that may work all the way from, say, ovarian cancer through to Hodgkin lymphoma.

So, the clinical opportunities, based on our ability to identify the right patients to get treated, and conducting the right trial, and choosing the right combinations -- we can do combinations -- is the future beyond monotherapy is extremely broad. And if you look at the Merck development program, our lead -- if it was in melanoma, we'd follow that with a robust plan in non-small cell lung cancer. It just achieved approval in head and

neck cancer. We have a robust plan for bladder cancer, for triple-negative breast cancer, Hodgkin lymphoma, hepatocellular carcinoma, esophageal carcinoma, gastric cancer.

So, if you look at what I'm describing, and if (inaudible), the clinical utility of something like pembrolizumab, that can be broadly applied. And it soon becomes -- I think we see it as foundational and as the backbone potentially of many therapies. So, the addressable population of patients obviously under the sort of construct that I'm describing is large. And take lung cancer by itself is a dominant cancer. There are many, many thousands of patients who will benefit. What that turns into in terms of potential monetary value, I think I'll ask Teri to comment on.

But, we are choosing to develop pembrolizumab appropriately in multiple different // where we see a strong signal. And that translates into hopefully many patients benefiting.

Teri Loxam - *Merck & Co. - Vice President, Investor Relations*

And I think it's difficult to put a number on what this opportunity could be, for a number of reasons, one being that, as Roger stated, this is very early, and it's never been seen before for a drug to be so active across so many tumor types. So, it is really difficult for even us internally to be able to put a revenue number on that.

Analyst estimates for the market size, not just from us but across the market, I mean, we've seen $10 billion, $20 billion, $30 billion for the IO space across many different market models that the analysts have put together. We can't comment one way or another kind of where we think it all lands because we really just don't know. I think the important part is that it will be a very big opportunity.

Merck is very well positioned to be a very big part of that opportunity, especially given some of our recent news around first line lung cancer, which is a very large opportunity in and of itself. And so, we'll see where it goes, but it's an important product for the Company, and we've often described it as kind of a pipeline within a product. And it's definitely something that we're pursuing pretty strongly.

David Maris - *Wells Fargo - Analyst*

One of the things that you mentioned in your opening comments is that -- and you're ultimately looking at combination therapy if it turns out to be [the case]. Most people believe that combination therapy is just -- that's where it will be. Is there a reason to think that maybe that won't be the case, or that patients won't take the trade-off of what the combination therapy might entail?

Roger Dansey - *Merck & Co. - Senior VP, Clinical Research*

That's a great question. So, take, for example, melanoma. We've established pembrolizumab as a standard of care for [ipilimumab]-naive patients [based] on monotherapy. And the results in that monotherapy population are excellent. Will a combination beat that in terms of something like overall survival? We don't yet know. But, certainly the monotherapy has a very favorable sort of safety, tolerability profile, is readily administered, and has a very specific safety profile related to immunotherapy but doesn't necessarily overlap or sort of cross-contaminate other potential combinations.

We've taken in the monotherapy space -- we've taken a biomarker-based approach to try and increase and identify the patients that are most likely to benefit. And what that has translated into is us being able to beat standard of care. So, again, lung cancer is a good example, where with (inaudible), which was in a second line non-small cell lung cancer population, we were able to beat -- to demonstrate superior overall survival against a drug like docetaxel. Although the results are not public, as you know, we've [read out] on Keynote 24, which is a front line monotherapy population enriched now to a 50% [cut point] where we have, in fact, consistently shown really excellent outcomes all the way from an advanced population up to front line, and with randomized trial I think confirms that.

So, for monotherapy, for patients with cancer who are awfully ill and maybe have advanced disease, monotherapy's an attractive option, not only from an efficacy perspective but also from a tolerability and a safety perspective. And the place of monotherapy is well established in melanoma.

The place of monotherapy is pretty well established in non-small cell lung cancer. We're going to add to that in front line. But, obviously combinations represent an alternative treatment option.

And so, in a non-biomarker-based approach, looking to test a combination therapy, again, and I can't really give examples, they've already begun chemotherapy, pembrolizumab combination trials, to see if we can, in fact, improve the outcome for the entire population. But, the monotherapy biomarker-based approach is a very strong one, and I think we have really good data to support the clinical benefit.

David Maris - *Wells Fargo - Analyst*

So, in your discussions, have you -- do you think you're at the point where you have an understand of where it might not work? And where might those areas be?

Roger Dansey - *Merck & Co. - Senior VP, Clinical Research*

Specifically in a -- by tumor type. It's early. So, for example, if one takes a myeloma, I think we were aware of data from other companies demonstrating not too much (inaudible) activity, and then when we combined our drug with an (inaudible) together with (inaudible), [serolinumide] or (inaudible), we got excellent responses.

I think it's hard to shut the door on anything particular because even if a monotherapy plan doesn't necessarily produce significant results, it's quite possible that a combination will. I don't think we've shut -- we have a very broad-based plan, which doesn't exclude specifically any disease at this point.

David Maris - *Wells Fargo - Analyst*

Are there any trials that are ongoing where you say, well, if we have the answer to that, we'll know the answer to four or five other tumor types, or is it just going to be one by one?

Roger Dansey - *Merck & Co. - Senior VP, Clinical Research*

I think as a principle, the question of combination of a PD-1 inhibitor with chemotherapy is a general principle, so to be answered. Obviously one can't extrapolate from one trial to the other. But, if one study read out positive in one disease, it would give one some encouragement that other trials may point in that direction. But, in the end, it is disease by disease, trial by trial, in terms of understanding what the outcomes are.

David Maris - *Wells Fargo - Analyst*

Now, what are the next catalysts between now and a year from now that you think are the highest priority catalysts?

Roger Dansey - *Merck & Co. - Senior VP, Clinical Research*

Let me pause and think a little bit about that answer. You mean from a clinical development perspective?

David Maris - *Wells Fargo - Analyst*

Yes, data readouts.

Roger Dansey - *Merck & Co. - Senior VP, Clinical Research*

Data readouts. Well, obviously there's a lot of focus in lung cancer. We will have some more information on chemotherapy plus pembrolizumab later in the year. Our chemotherapy combination trials have got specific plans that will read out over the next while. [Gad], of course, and immunotherapy combination will also be potentially informative.

But, I think for us, from a catalyst perspective, we had a broad swath of combination trials that are going on that are essentially signal detection with collaborators and partners and so on. And in terms of making decisions about what would we do next, I mean, we base our decisions on data. So, we see a strong signal of efficacy and acceptable safety, that would be a catalyst for us to proceed internally with a further development plan.

So, I think it's the -- and this term I think has been coined before -- we're likely to see a wall of data coming in the next while, because there was so much activity going on. And my expectation is that we will be informed significantly by those readouts as to what the next step will be. And then, obviously we have our internal pipeline, which would be a catalyst for proceeding to something that would have a registration event if one of the internal pipeline molecules in combination, say, with KEYTRUDA read out something positive.

Teri Loxam - *Merck & Co. - Vice President, Investor Relations*

And if you want to think through kind of the investor catalysts, right, from an external perspective, [actually ESMO] is coming up in October, and it's a very big, important meeting for Merck, for KEYTRUDA. We obviously have the first time that you will see the first-line lung data from Keynote 24 will be presented at ESMO, and I think that's probably one of the biggest catalysts for the Company at this time.

In addition, we've got, I want to say, data across 12 different tumor types. We've got a [late breaker] for front-line bladder, for instance. That'll be really the first time that people see KEYTRUDA in bladder. We've got head and neck data. We've got other -- our other lung data. So, I think ESMO in and of itself is a really important meeting for Merck and a catalyst as well, in addition to a whole host of other trials that read out between now and 12 months from now. Those monotherapy and combo therapy, I think there's going to be a lot of catalysts out there that you'll be able to understand both KEYTRUDA and the opportunities in monotherapy and combination therapy over the next 12 months. There's a lot of data.

David Maris - *Wells Fargo - Analyst*

So, I've seen a lot of drug companies over the years, and usually the scientists with the winning products get pretty much an unlimited budget. Is there any -- are there any studies that, if you had an unlimited budget, that you would want to do that you're not doing?

Roger Dansey - *Merck & Co. - Senior VP, Clinical Research*

I think we have a pretty fully fleshed out development program at this point. And the Company's commitment to immuno-oncology is very significant. And I think if you did some cost comparisons potentially, we probably have the biggest and the (inaudible) program currently in existence.

Teri Loxam - *Merck & Co. - Vice President, Investor Relations*

I think from -- as we think through it at the corporate level and we look at the R&D budget, KEYTRUDA's a very important product, and the IO space is moving very, very quickly. So, it's something that, as a company, we have prioritized resources to KEYTRUDA so that we can be ahead of the curve, and so that we can fully build out the program across.

We've got over 300 clinical trials ongoing for KEYTRUDA across 30 different tumor types. And because it's moving so quickly, it is important to fund that. We are doing everything we can within the Company then to be prioritizing across the rest of our portfolio, so making those trade-offs more so than we ever have before to make sure that we can appropriately fund KEYTRUDA, keep the rest of our programs moving forward, but really taking a critical look at can something be pushed six months and not be detrimental, and will that allow a difference, another arm put in a KEYTRUDA

trial, for instance. We're having those types of conversations within the Company, but it's important for us to make sure KEYTRUDA's successful over the long-term.

David Maris - *Wells Fargo - Analyst*

So, let's talk about competitors for a second. What data in the last six months have you seen from a competitor where you said, wow, that's really interesting? And what's on your radar for competitor data that you really want to see?

Roger Dansey - *Merck & Co. - Senior VP, Clinical Research*

Well, so for [ESMO], we are very interested in seeing Bristol-Meyers data, CheckMate 26. There is some analogy between 24 and 26 in that it's a front line monotherapy biomarker-based trial. Obviously there are -- different cut points have been chosen, but I think they're very interested in trying to understand, interpret the data.

We're also interested in seeing data from Roche. There's a lung trial, I believe, that will be presented, Oak, that will be very informative. So, going forward, those would be the two sort of most near-term data points that I'm aware of.

Going backwards, at ASCO, there were obviously interesting data presented again around IO combinations in lung, all small data sets, and so obviously the caveat around interpretation of this data is best in a (inaudible) data set. And in 2017, obviously a lot of these trials are driven by event numbers, so timing is not clear, but I do believe there'll be a readout potentially from AstraZeneca on a PDL-1 combination with a [PTA-4] in lung cancer. So, that could be an interesting thing to look at.

It is [always] (inaudible). It's complicated to do the cross-trial comparisons. Studies are set up in a randomized [context for an expansion] to ensure that there isn't variability, or you can try and reduce the amount of variability. So, cross-trial comparisons do have their limitations, but obviously it's important to look at other data.

David Maris - *Wells Fargo - Analyst*

Let me also turn it over to any questions from the audience, if there are any. There's a microphone in the back. Have we stunned you all into silence? [I can't] goad you into something.

So, feedback on pricing, I know that's not your area, and Teri, maybe you can give us the perspective that you've heard. But, I'm sure you've heard from -- at least internally from payers' groups, but maybe externally from physicians, has there been any pushback? Is there pricing sensitivity?

Teri Loxam - *Merck & Co. - Vice President, Investor Relations*

I mean, there's always pricing sensitivity, right? You have to make sure that you've got the right clinical data to be able to show the benefit risk analysis and the value of the product. And I think our clinical trials are designed in order to be able to put that value proposition forward. So, from that perspective, KEYTRUDA has shown a significant value proposition. And because of that, I think we haven't seen too much pushback yet. Globally, obviously, pricing is becoming a bigger topic, and healthcare spending in general obviously is difficult across the globe.

So, it's something that we pay attention to. I think if we're talking just about KEYTRUDA, the real question is going to come down around when combinations start rolling out, how does that work, and how does that work both within the US pricing system, where potentially the two components of the combination, one might be through a part B system and one might be through a part D system, how does that play out? Does one plus one equal two? Or is there some other way to price these combinations?

As we go forward, as well, across different tumor types, how does that play out when you're trying to launch a drug in a small indication versus a very large indication? I don't think that we have those answers, and I think collectively as an industry, it's going to be something that we'll all be playing out over time.

But, I think, at the end of the day, what we've been able to see consistently is that, if you can show the data and the clinical benefit, and show that value proposition, then you can generally make sure that it makes financial sense. And that is really, at Merck, the foundation of what we do, is making sure that we're bringing forth products that can show that value.

David Maris - *Wells Fargo - Analyst*

Do you think that we're still in the position where survival wins, numeric advantage and survival win, or are we at the point where the dialogue for -- well, what's a meaningful difference in survival if you have two successful drugs in the same tumor type, and the survival difference is -- and so, first, what is the meaningful difference, in your opinion? And are we ready for that dialogue of, well, this is what it means, the (inaudible) preference, I'm going for the longest survival. I don't care what it costs. But, is that part of the debate, or no, that's not really -- we're still in the longest survival wins?

Roger Dansey - *Merck & Co. - Senior VP, Clinical Research*

So, [that's all now], and I don't think things have changed. Survival remains the gold standard. It is going to get more complicated, because as the availability of drugs like pembrolizumab and others start to play out, the ability in a controlled environment, like a clinical trial, to demonstrate a long-term outcome like survival may be more complex because of unintended or unplanned crossover to another agent that's active. But, it remains the gold standard.

And obviously, for every -- it almost goes disease -- by some diseases, for example myeloma would be an example. To show an overall survival signal takes a very long time, so more proximal [surrogate] (inaudible) are acceptable for diseases that are moving fast, survival is more likely something you'd be able to show for adjuvant trials. Survival is an important outcome.

So, this is quite a nuanced conversation around survival, but it still remains the key outcome. If we can demonstrate it, I think it does trump pretty much everything else.

David Maris - *Wells Fargo - Analyst*

Okay. For me it does, as well. So, if we talk a little bit about first line lung, KEYTRUDA's data was clearly better than Optivo's. Does that change your strategy at all in development plans? Or is it just a confirmation of what you suspected all along?

Roger Dansey - *Merck & Co. - Senior VP, Clinical Research*

Yes. so, if you look at the data we presented with KEYTRUDA in lung cancer, it's remarkably stable, so all the way from Keynote 1, which was that very small phase one trial, which was planned initially to enroll 32 patients, also ended up 1,000 patients with multiple approvals. We were able to demonstrate, using a biomarker-based approach, identifying the patients, [people] most likely to benefit, that both in second line-plus and in first line in their uncontrolled trial in Keynote 1, results looked very encouraging.

Then, Keynote 10 comes along in a randomized comparison to standard of care using again, a biomarker-based approach. We show improvements in survival. We've now recapitulated [that] results in front line with a higher cut point, using the 50% cut point, but again, monotherapy against standard of care. So, our own data internally is very consistent based on our biomarker choices.

In terms of what do we do, going forward, we already have plans in place, as I've mentioned, in chemotherapy combinations to see if we can improve the outcome combining pembro with chemo. We continue to look at other novel combinations in lung cancer, for example, the [IDO] inhibitors under evaluation. We presented some data at ASCO looking at pembro and a dose of ipilimumab at one milligram per kilogram, four doses. And that data is potentially informative.

And I think we are continually scanning the environment, both internal and external, trying to make the best possible choice for the next move, whatever that may be. And it's all data-driven. So, I don't think any of our plans are sort of locked and loaded, and that's the end, we'll do no more. I think every time we see an important signal with good safety and potentially significant efficacy, it's something we see as we consider should that be taken forward.

And a good example of that approach would be, say, melanoma, where we've clearly demonstrated tremendous benefit in monotherapy, but we're not stopping there. So, we have a combination both with the (inaudible) [engines], oncolytic virus, a combination trial that's running in phase three. We have a combination trial with, [in fact], IDO-1 inhibitor in phase three, both of those based on what we thought were early and strong signals to try and improve the outcome further.

And I think that's a good model for how we approach, and how we will approach other tumors. We'll choose based on data, what the best possible combination we think is, and/or combinations we think we should take forward. And it's an evolving [profit].

David Maris - *Wells Fargo - Analyst*

So, one of the things I always ask companies is -- and I think anyone who works for a company of more than maybe five people, there's always an interesting answer of, gosh, how much time do you have? Finish this sentence. If people really knew "blank," they'd really be surprised -- about the pipeline, about what you're working on. I mean, I don't want you to tell us something personal, "I can juggle," something like that.

Roger Dansey - *Merck & Co. - Senior VP, Clinical Research*

I think they'd be excited, data. We're obviously seeing information all the time. It's remarkable. And we're in almost a revolution from a therapeutic perspective. And the future -- I don't want to hyperbolize this too much, but it feels like the sky is the limit, with so much innovative science, such clever thinking and strong scientific underpinnings for potential future combinations and approaches, it's remarkable. If you synthesize all of that together and say what could the future look like, it really looks very encouraging.

David Maris - *Wells Fargo - Analyst*

So, when you think about that runway, do you think that's a -- oh, gosh, because when people say the future's really exciting, sometimes they mean the next three years.

Roger Dansey - *Merck & Co. - Senior VP, Clinical Research*

I think it's now, and it's three and five and beyond. I think this is a continuous -- the readouts for data are going to be -- they're already beginning. They have begun, and they will continue. This data flow will continue. And that will inform future plans.

Teri Loxam - *Merck & Co. - Vice President, Investor Relations*

And David, I was just going to add to what people, and investors in particular, have found surprising as they've started to [dig into] market, especially our oncology program, is the talent that we have amassed, both on the commercial and the R&D side, both from within the organization but as well from outside the organization. And we've brought people in, the experts from across a number of pharmaceutical companies, Roger being

one of them, coming in that has a wealth of oncology experience over just a career, have come to Merck to work on the KEYTRUDA program because of how exciting this is.

And I think a lot of investors, once they start digging in, are surprised by the talent that we've got working on this program. And one of the reasons that we have been able to execute so well is because of that talent that we've been able to bring in.

David Maris - *Wells Fargo - Analyst*

Yes, this is an odd question, but if you couldn't work on KEYTRUDA, but you could work on another novel program that you're aware of in oncology at Merck, what would it be?

Roger Dansey - *Merck & Co. - Senior VP, Clinical Research*

We have a really -- I'm a late-stage developer, so my strong desire is to get drugs approved, and that's where I get most of my gratification from. But, from an early perspective, we have lots of interesting targets, I mean lots of interesting possibilities. It goes all the way from a recent deal signed I think with Mederma around personalized RNA vaccines, to Ablynx with nanobodies, to pipeline molecules, such as things like [GIDDA]. And I can't select one. I think they're all interesting.

Unidentified Audience Member

Does the recent Bristol and your data make you more interested in, just as a insurance mechanism, do first-line trials with CTLA-4, more pivotal trials with that mechanism?

Roger Dansey - *Merck & Co. - Senior VP, Clinical Research*

I think our position right now is we continue -- we are continuously evaluating. And the development plans will evolve for (inaudible). So, I think it'll be helpful for us to see the monotherapy trial. We understand the interest around CTLA-4. It's one way to go, and it's something that we had already looked at. We've looked at [IPI] and pembro (inaudible). We've presented some data with IPI and pembro in [LAN]. So, it's obviously part of our consideration.

David Maris - *Wells Fargo - Analyst*

Well, great. I want to thank Roger and Teri for their participation. And it's always great to speak to someone on the front lines of something so exciting. The industry gets such a bad rap from so many, and these are the stories that really need to be told about lifesaving medications that are revolutionizing the treatments. So, thank you for all the work that -- thank you for your participation.

Roger Dansey - *Merck & Co. - Senior VP, Clinical Research*

Sure. Thank you.
