REFINITIV STREETEVENTS

EDITED TRANSCRIPT

MRK.N - Merck & Co Inc at ASCO Annual Meeting

EVENT DATE/TIME: JUNE 07, 2022 / 12:00PM GMT

REFINITIV

CORPORATE PARTICIPANTS

Dean Y. Li *Merck & Co., Inc. - Executive VP & President of Merck Research Laboratories*

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

Eric H. Rubin *Merck & Co., Inc. - SVP of Global Clinical Oncology & Early-stage Oncology*

Jannie Oosthuizen *Merck & Co., Inc. - Senior VP & President Merck U.S. Human Health*

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

CONFERENCE CALL PARTICIPANTS

Chris Shibutani *Goldman Sachs Group, Inc., Research Division - Research Analyst*

Daina Michelle Graybosch *SVB Securities LLC, Research Division - Senior MD of Immuno-Oncology and Senior Research Analyst*

Evan David Seigerman *BMO Capital Markets Equity Research - MD & Senior BioPharma Research Analyst*

Mohit Bansal *Wells Fargo Securities, LLC, Research Division - Senior Equity Analyst*

Seamus Christopher Fernandez *Guggenheim Securities, LLC, Research Division - Senior Analyst of Global Pharmaceuticals*

Stephen Michael Scala *Cowen and Company, LLC, Research Division - MD & Senior Research Analyst*

Terence C. Flynn *Morgan Stanley, Research Division - Equity Analyst*

PRESENTATION

Editor

This transcript is incomplete due to a portion of the audio being unavailable. The following summary is not a verbatim representation of this missing audio portion and has been provided by the Company.

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

[Good morning. I am Peter Dannenbaum, head of investor relations. Welcome to Merck's ASCO investor event. Thank you for joining us today, both those here in the room in Chicago and those on the webcast.

Presenting from Merck today are Dr. Dean Li, President of Merck Research Labs; Dr. Eliav Barr, Head of Global Clinical Development and Chief Medical Officer; Dr. Eric Rubin, Head of Early-Stage Oncology Clinical Development; and Jannie Oosthuizen, President of U.S. Human Health.

Our agenda includes roughly 30 minutes of upfront remarks, followed by 30 minutes of Q&A. Those tuning in virtually can submit questions via the webcast or e-mail me directly at peter.dannenbaum@merck.com.

Joining for the Q&A session will be Dr. Scot Ebbinghaus and Dr. Greg Lubinecki from our Oncology clinical development team. Joining via a phone line is Dr. Roy Baynes.

We will be making forward looking statements and I encourage you to read slide 4 and the risk factors contained in our 10-K.]

With that, I'm going to hand it over to Dean.

Editor

End of non-verbatim summary.

Dean Y. Li - *Merck & Co., Inc. - Executive VP & President of Merck Research Laboratories*

(technical difficulty) to be here today. As we discussed, Eliav will outline the progress made since the last ASCO sort of investor meeting we had in 2021. Since that time, I just reemphasize, I think there's 12 U.S. approvals across 8 tumor types since the last time we had an event like this. Eric will update a subset of the 20 novel mechanisms that we are advancing as we seek to advance and diversify our impact on oncology. And then Jannie will provide a commercial landscape of our ability to touch the lives of patients and their families. And then Scot and Greg, who will provide color and just through by early morning discussion with some of you, some of the questions that were asked at me, Scot and Greg would be perfect people to give even more color to some of those questions.

So this is what we have from a sort of clinical development standpoint. We have a rich set of clinical experiments composed of internal programs and clinical trials with external partners. If you look on the left side, many of these studies are often in combination therapies. And what we're trying to do is learn what are the best mechanisms on their own or in combination that can move the needle for patients. And as you see in the top right corner, we are aggressively moving into earlier stages of cancers where the opportunity to change the course of cancer is profound. I also want to highlight that many of these clinical trials that we lay out when we say 1,300 greater than 1,750 are really ones that are both internal and are in partnership with others. And those readouts from these clinical studies are what fuel our business development transactions.

So our progress to date continues to inspire us to achieve more. We seek to expand and listed here as we seek to expand into new tumor types, and we've done that successfully just over this past year. We are very interested in extending our reach from late-stage metastatic disease to early stages of cancers. I would just emphasize when we -- moving into earlier-stage cancers and you'll see many of those readouts, those are readouts that come from clinical trials that were begun quite some years ago simply because it takes longer for the early stages to mature. And then clearly, we need to deepen the response in combination with other IO agents and that range from checkpoint inhibitor for T cells and myeloid cells to cytokines and innate activators. We also want to deepen our response in combination with non-IO agents like chemo, Lynparza, Lenvima and to many other cancer intrinsic mechanisms, some of which Eric will touch.

And with that, I will now turn to Eliav, who will recount some of the progress we've made since the last 2021 ASCO meeting. Eliav?

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

Good morning, everyone, and thanks, Dean. So Merck Oncology has had a really productive year since the last ASCO. We've continued to deliver on our commitment to improve patient outcomes. As being noted, we've received 12 U.S. approvals, including 6 in metastatic stage cancers across 8 different tumor types, and you can see those here.

In addition, KEYTRUDA was approved for treatment in adjuvant therapy following nephrectomy in certain patients with renal cell cancer and in triple-negative breast cancer in locally advanced cutaneous squamous cell cancer and as adjuvant treatment following surgery for high-risk Stage IIb or IIc melanoma. Lynparza was approved as adjuvant therapy for certain patients with HER2-negative high-risk early breast cancer with BRCA germline mutations, who received neoadjuvant chemotherapies. You can see that we're moving into earlier lines of therapy and combining our assets with surgery to hopefully help patients achieve cure.

We've also had a new molecular entity, WELIREG, which is a first-in-class HIF-2 alpha inhibitor for treatment of adult patients with certain kinds of von Hippel Lindau-related tumors. This was approved. And as Eric will point out, there'll be other opportunities to look at this very important and exciting new molecular entity.

We also have had 3 readouts of pivotal trials, including KEYNOTE-394, which showed KEYTRUDA improving OS versus placebo in patients with advanced HCC previously treated with sorafenib. So a really important finding for patients with hepatocellular cancer.

We've also had, of course, KEYNOTE-091, which -- for which one of the dual primary endpoints showed the KEYTRUDA improved disease-free survival versus placebo as adjuvant therapy in certain types of Stage Ib to IIIa non-small cell lung cancer following resection, regardless of PD-L1 expression. Now the trial will continue to analyze disease-free survival in patients who express high levels of PD-L1, so TPS greater than 50%, which was the other dual primary endpoint of the study, which had not yet met its statistical significance based on the prespecified plan, but we will have further analysis of that.

And then finally, considering Lynparza again, we had the PROpel study, which showed that Lynparza with abiraterone reduced the risk of disease progression or death versus abiraterone alone in first-line metastatic castrate-resistant prostate cancer, regardless of biomarker status. This is a really important finding in a very large set of patients with prostate cancer and a very exciting opportunity for those patients to improve outcomes.

Now over the years, we've made I think some really exciting presentations and published some important results at several meetings, including studies that forming the basis of new indications for KEYTRUDA and evaluation of new compounds that are coming through the pipeline. At this year's ASCO, we really reinforced the breadth and depth of the oncology portfolio. We had over 150 abstracts presented with the results of our compounds; about 2/3 of them were with KEYTRUDA. And these data emphasize the broad nature of our oncology program, the long-term durability of responses we're observing for patients and the continued progress into earlier lines -- into early-stage settings.

Overall, we're really confident in our ability to continue this momentum and to improve patient outcomes. And let me review some of those abstracts in a bit more detail to explain what we were able to show. So first and foremost, KEYNOTE-716, which evaluated pembro or placebo as adjuvant therapy among 976 patients, 12 years or older who had undergone complete recession for Stage IIb or IIc melanoma. As published recently in Lancet, administration of pembrolizumab, KEYTRUDA, reduced the risk of death for local, regional or distant recurrence of Stage IIb or IIIc melanoma by 35% compared with placebo. The study continued to collect further data, including distant metastasis-free survival, which is a key secondary endpoint.

Now, why are we so excited about these results that we presented? As you know, distant metastasis, especially the brain, liver, lung or soft tissues can really pretend a poor prognosis for patients. This is particularly true in melanoma. And here, we were able to demonstrate that KEYTRUDA reduced the risk of these types of recurrences by 36%. And at a median follow-up of 27.4 months, we also showed improved -- sustained improvement in the primary endpoint of the study, which was recurrence when we compared to placebo. And it was exciting to see that the 24-month recurrence-free survival rates were 81.2% for KEYTRUDA and substantially lower for placebo. So these data add to the body of evidence that KEYTRUDA works very well as adjuvant therapy for patients with earlier stage melanoma, and it builds on the positive results that we've already seen in -- for KEYTRUDA in earlier stages of cancer, especially those where there's a hope for period of intent.

Now, we also continue to make progress in earlier stage setting. We all know that patients who are diagnosed early and receive timely treatment are generally more likely to survive and experience an improved quality of life. We've successfully shown the efficacy of KEYTRUDA in reducing recurrent disease in certain earlier-stage settings, one of which I just mentioned. Now we've extended our observations with exploratory analysis to fill the details of a bunch of studies that we already reported out, but have really important findings that deepen the understanding of the value of KEYTRUDA in these settings.

So for example, on the left, if you take a look at KEYNOTE-522, this is our study of perioperative pembrolizumab in high-risk triple-negative breast cancer. We showed that event-free survival benefit of pembrolizumab may be based on both the preoperative and postoperative antitumor effects. So this is really important as there has been questions about whether giving the drug after surgery adds value. And I think we are able now to provide data that demonstrate that.

The middle is KEYNOTE-564, which showed the efficacy of KEYTRUDA's adjuvant therapy post nephrectomy in certain kinds of renal cell patients -- renal cell cancer patients. And here, we show the continued benefit of therapy, including benefit with distant metastasis-free survival, the same kind of endpoint that I described for melanoma where we're looking at really bad things like brain mets and lung mets and so on, as well as the need for second therapy and the time to -- the progression-free survival after that second therapy. So that durability of efficacy that we would anticipate with immunotherapy is there, and now we're able to demonstrate that and the study will continue on to evaluate endpoints such as OS.

And then on the right, KEYNOTE-091, again, we talked a little bit about that before. This study evaluated the efficacy of KEYTRUDA's adjuvant therapy following resection of certain stage Ib to IIIa non-small cell lung cancer. We were able to provide further efficacy findings in key subgroups, including those related to surgery, disease burden, the type of adjuvant chemotherapy. All of the results were consistent with respect to disease-free survival at that dual primary endpoint for all comers. And so again, we're building a body of evidence in non-small cell lung cancer for the benefit of pembrolizumab. Here is adjuvant therapy, and I would remind you that there is a further study. Then we'll look at pembrolizumab as neoadjuvant and adjuvant. And we're excited to share those data when they become available.

Finally, one of the things that we've begun to see is the fruits of a lot of work to rationally design new approaches to investigate the treatment of cancer. And one of these approaches is to explore ways to deepen the immune response to KEYTRUDA through co-formulated combinations with antibodies that target complementary new pathways. And a good example of that is favezelimab, which is our investigational anti-LAG-3 therapy.

Here at ASCO, we presented data on 2 cohorts from the Phase I/II study that evaluated the safety findings of combining favezelimab with pembrolizumab in patients with relapsed or refractory classical Hodgkin's lymphoma who had not received prior anti-PD-1 therapy. So that was Cohort 1 and those who had already progressed despite being -- having therapy with anti-PD-1 drugs. And I'd point out that pembrolizumab has shown great efficacy as in patients with relapsed/refractory classical Hodgkin's lymphoma.

In both cohorts in the Phase I/IIb study, the co-formulated drugs showed manageable safety profile and demonstrated antitumor activity in the 2 different kinds of patients. Of particularly notable in my mind is the efficacy that was observed in those who had already failed single PD-1 therapy where we had encouraging objective response rates of 30%.

Now finally, we had additional presentations of both KEYTRUDA and WELIREG demonstrating, again, the efficacy is being maintained over time and providing durable benefit to patients. And we followed up on these studies with Phase III evaluations. And you could see the 3 trials that are described here. So for inoperable Stage III non-small cell lung cancer, we were conducting KEYVIBE-012 and KEYVIBE-06, which follows up on the results here of KEYNOTE-799 in the Stage III non-small cell lung cancer. And we're looking at our new combinations with KEYNOTE-056 evaluating our co-formulated pembrolizumab-vibostolimab therapy.

For the first-line HCC, which is in the middle, we continue to see durable antitumor activity for KEYTRUDA based on KEYNOTE-224 and we'll be following that up with other studies, including with Lenvima. And then for WELIREG, we have an extensive program that takes the exciting results in VHL disease-associated RCC and moves that into patients with sporadic renal cell cancer in order to determine whether the drug has efficacy in a broader population of RCC patients. So it's a very exciting program going forward.

And with that, I'll turn it to Eric. Thanks.

Eric H. Rubin - *Merck & Co., Inc. - SVP of Global Clinical Oncology & Early-stage Oncology*

Thanks, Eliav. So before I begin, I want to take a moment to reflect on the progress that's been made since the first presentation of interim Phase I data for KEYTRUDA at ASCO in 2012, 10 years almost to this day. That first poster included just 9 patients and it's been my privilege to have been involved in the development of this medicine and to see the practice-changing impact it's had on cancer.

KEYTRUDA has fundamentally changed the way we think about cancer and have set a high bar for ongoing development programs across our oncology pipeline. Our current pipeline today is guided by a deeper understanding of cancer biology and informed by insights from clinical evidence amassed over the past decade through the extensive KEYTRUDA clinical development program. We have a rich and deep pipeline of assets spanning all stages of development, targeting multiple aspects of cancer biology and immune-based pathways as well as leveraging new modalities and platforms. Eliav has already mentioned favezelimab, which is one of 3 ongoing Phase III IO-IO programs that we are studying as co-formulations with pembrolizumab. We have now advanced 5 candidates into Phase III studies largely over the past year, including favezelimab, vibostolimab, quavonlimab, zilovertamab vedotin, which is our anti-ROR1 antibody drug conjugate and, as Eliav mentioned, WELIREG, our HIF-2 alpha inhibitor.

Vibostolimab, favezelimab and quavonlimab are each developed internally by our scientists, and each is being evaluated for its potential to deepen responses that are observed with pembrolizumab and thereby extend benefit to more patients.

We also have successfully used business development to secure externally sourced assets that complement and augment our pipeline. One example is WELIREG, the first HIF-2 alpha inhibitor therapy, which received approval in August of 2021, only 2 years following the acquisition of Peloton Therapeutics. We're also advancing collaborations, evaluating novel cell-based therapies as well as T and NK cell engagers with A2, Artiva, GENX and Dragonfly.

At Merck, we follow the science. Taken together, we are advancing adverse pipeline of candidates that leverage biological insights gained from our deep expertise and large clinical data sets.

Now to an area of research that has been in the news recently, our anti-TIGIT program. Vibostolimab is a humanized anti-TIGIT monoclonal antibody that is designed to restore antitumor activity by blocking the TIGIT receptor from binding to its ligands, CD112 and CD115, thereby triggering key lymphocyte activation towards tumor cells. We are developing MK-764A, which is the co-formulation of vibostolimab and pembrolizumab, in a single vial currently delivered through one 30-minute infusion.

Vibostolimab is the only anti-TIGIT medicine that's been evaluated in combination with pembrolizumab in Phase III trials and builds upon the high bar set by KEYTRUDA in lung cancer, as the only anti-PD-1/L1 therapy to demonstrate an improvement in overall survival in 5 Phase III clinical trials. Encouraging signals we observed in preclinical and early studies with vibostolimab have informed the systematic development strategy for the co-formulation across tumors in 8 ongoing studies, including 4 Phase III trials in lung cancer, all of which are designed to provide clear answers to the incremental benefit of the antibody when added to pembrolizumab.

Notably, in the KEYVIBE-003 study, we're enrolling TPS to PD-L1 TPS greater than 1% patients, not just TPS greater than 50%. We wish to evaluate the effect size for adding an anti-TIGIT antibody in the TPS greater than 1% as well as the TPS greater than 50% non-small cell lung cancer populations.

We've taken a targeted and thoughtful approach in how we proceed with the evaluation of our checkpoint modulators and continue to follow the science to inform which combinations to advance with a focus on areas of high unmet need. Based on the favezelimab data presented during the conference and discussed earlier by Eliav, we plan to initiate a second Phase III study of favezelimab in patients with relapsed/refractory Hodgkin's lymphoma who've progressed on prior anti-PD-1 therapy. There's currently no standard of care for these patients. We also have an ongoing Phase III study of co-formulation in PD-L1 positive microsatellite stable colorectal cancer, which is an area of significant unmet need as colorectal cancer is the third most common cause of cancer death and 96% of metastatic colorectal cancer is classified as microsatellite stable.

We will continue to leverage insights and clinical learnings across our oncology development program to help inform additional development decisions for the favezelimab and pembrolizumab co-formulation. Based upon the efficacy observed with CTLA-4 targeted therapy as monotherapy in renal cell cancer, our Phase III study with our CTLA-4 agent is evaluating quavonlimab as a co-formulation with pembrolizumab plus Lenvima, as we look to build on the strong foundation established by KEYTRUDA in combination with Lenvima in the first-line advanced renal carcinoma setting.

Following on from the strong long-term data Eliav described, WELIREG is the first HIF-2 alpha to come to market and the first systemic treatment for VHL-associated tumors. It is based on the Nobel Prize winning science pioneered by Bill Kaelin, Gregg Semenza and Peter Ratcliffe. Building on the establishment of clinical proof of concept in VHL that was central to the FDA approval for WELIREG for the treatment of patients with certain VHL related tumors, we are now evaluating its potential in sporadic renal carcinomas. VHL dysregulation and abnormalities are quite common. In fact, the majority of sporadic renal cell cancers have this abnormality. Based upon this, we've extended the program very rapidly through a series of registrational-enabling trials into different lines of therapy in the adjuvant setting as well as either in combination with KEYTRUDA or as a triplet with Lenvima. We look forward to sharing readouts from these as data become available.

From the beginning, we approached the evaluation of KEYTRUDA with an open mind, seeking to maximize our understanding of monotherapy across various cancers using precision medicine tools to identify those patients most likely to benefit while also recognizing that for some patients, a combination approach would likely be needed. Our pursuit of first a biomarker and then a companion diagnostic for the ligand PD-L1 particularly in lung cancer as a means to inform treatment decision reflects strong patient focus. This strategy ultimately led us to evaluate novel combinations incorporating chemotherapy and culminated in the practice-changing results from KEYNOTE-024 and KEYNOTE-189 studies.

We've continued to build on this legacy of biomarker-driven development. Our proven track record of developing precision medicine strategies to inform treatment and enable better outcomes as evident in our 14 biomarker-driven indications and 2 tissue-agnostic approvals, including the first tissue-agnostic approval in the field for MSI, we also have the TMB high to mutational burden high tissue agnostic approval. The development of biomarkers beyond BRCA to predict response to Lynparza also provides a good example of the need to follow the science and further demonstrates our leadership in precision medicine with indications that leverage HRR and HRD biomarkers to identify patients most likely to benefit.

And more recently, WELIREG represents our company's commitment to build out a compelling portfolio of treatment options for patients, many of which are targeted therapies and guided by biomarker measurement. We're also looking at mutations beyond VHL that we think are important in the HIF-2 alpha pathway to help inform additional patient populations that might benefit.

In summary, we are leveraging the immense data and insights gained from KEYTRUDA, Lynparza and Lenvima to build and advance a growing portfolio of innovative early and late-stage oncology candidates across our pipeline. New technologies and our deeper understanding of cancer biology are fueling innovations in cancer diagnosis and treatment. We routinely conduct next-gen sequencing and RNA sequencing by our database of patient biopsies to better understand resistance and potential new targets.

Through our extensive external collaborations network and partnerships, including those involving large and geographically diverse clinical genomic databases, we are accelerating innovations and discoveries that will have a profound effect on the patient outcomes in the treatment of cancer.

With that, I will turn it to Jannie to provide a commercial update.

Jannie Oosthuizen - *Merck & Co., Inc. - Senior VP & President Merck U.S. Human Health*

Thank you, Eric, and good morning, everybody. It's good to be with you. Thank you for joining us this morning. So I'm excited to highlight how we believe the data and ongoing efforts to address unmet patient need continues to drive significant commercial opportunity and growth for Merck. This slide is a reminder of our broad oncology portfolio and the progress we have made since ASCO 2021.

In particular, since last ASCO, we received FDA approval for WELIREG, a first-in-class HIF-2 alpha inhibitor with strong growth potential. Across the portfolio, we have seen an increase in the number of approved indications, tumor types and the number of patients treated. Particularly, the number of patients treated exemplifies the impact that we are having on patients with these expansion into tumors and lines of therapy and across the product portfolio. For KEYTRUDA, we currently have more than 30 U.S. indications, the most of any oncology medicine which we anticipate doubling in the coming years. Another important KEYTRUDA milestone is that we have reached the 1 million commercial patients and are on track to probably reach 2 million patients by the end of 2024.

We are creating meaningful impact and transforming the clinical landscape in the earlier-stage setting with 7 approved indications to date. And last year at ASCO, we only had 3 approvals in the early-stage setting, so 4 additional ones leading up to this ASCO. I want to particularly highlight the impact that the KEYNOTE-522 regimen is having for patients with triple-negative breast cancer, which, as we all know, has the highest risk of recurrence within the first 5 years after diagnosis and is associated with worse outcomes compared to other forms of breast cancer. Looking ahead, there are important readouts coming up, including 3 in lung with KEYNOTE-091, KEYNOTE-671 and KEYNOTE-867, and 2 in head and neck with KEYNOTE-412 and KEYNOTE-698. As we evaluate this horizon, we anticipate the early stage setting to reach roughly 25% of our total KEYTRUDA revenue by 2025.

With the wave of new indications in the early-stage setting, we realized that approvals alone will not transform patient care. It requires a concerted effort to ensure we can reach and provide access to eligible patients. To that extent, we are working to ensure the full scale and capabilities of the organization -- the commercial organization are meeting the needs of our customers by delivering highly relevant information to them when they need it and in the channel that they prefer. We have learned how important it is to innovate both scientifically and commercially. An example is our ongoing clinical development of a subcutaneous formulation of KEYTRUDA to be of particular importance in the early-stage setting and our approach to a digitally enabled commercial model that will continue to support excellent execution and take us into the future.

As Eric already provided a nice introduction to WELIREG, I wanted to iterate a few key points. WELIREG is the first HIF-2 alpha inhibitor to come to market. It is the first therapy targeting a gene transcription factor, which developed on the back of Nobel Prize-winning science, and is the first systemic treatment for VHL-associated tumors. It is also a treatment -- a testament to our successful business development endeavors. In 2 months, we will hit our 1-year anniversary of the WELIREG FDA approval. Ongoing execution is progressing well and adoption of the regimen is increasing steadily across quarters.

Unsurprisingly, much of the early usage is in the 40-or-so clinical centers of excellence for VHL disease, involving a multidisciplinary team in the U.S. We continue to see significant long-term potential with 4 Phase III trials addressing areas of high unmet patient need, including expanding into advanced RCC across various lines of treatment as both mono and combination offerings. We believe this medicine has blockbuster potential and are excited about its ability to help patients in need of new treatment options.

Our significant investment and broad clinical program in oncology are expected to result in more than 80 potential approvals between now and 2028, and you see that on the left-hand side of the slide, and the different colors to pick the different assets for which those indications will be added. As you have heard from Dean, Eliav and Eric, new tumor types, earlier lines of therapy, including adjuvant and neoadjuvant, new mechanisms, combinations and co-formulations will all be important growth drivers as we aspire to be the world's leading oncology company. On the right-hand side, you can see how our position in Oncology overall is forecasted to evolve over the next few years. I am very confident that our company is on track to become the leading Oncology company and to have an enduring and meaningful impact on patients' lives through this decade and beyond.

With that, I hand it over to Dan -- to Dean for their closing remarks.

Dean Y. Li - *Merck & Co., Inc. - Executive VP & President of Merck Research Laboratories*

Thank you, Jannie. So I hope this graphic is useful. At Merck, we continue to transform the landscape of cancer therapy. And what we have achieved to date continues to drive us to do more for the patients. And our team conducts a systematic science-led program aimed at harnessing the potential of a wide range of portfolio and pipeline assets. And they span internal and external innovation. They span IO mechanisms and targeted cancer mechanisms. They expand modalities ranging from small molecules to biologics to cell therapy and everything in between. And they span biomarker-driven as well as all-comer strategies. So we look forward to providing further updates throughout 2022.

I did want to close. Unfortunately, Roy because of what we would call Travel & Mayhem is not with us, he's on the line and he probably got win that we were going to do this. And so the Travel & Mayhem and the embarrassment that he sometimes feels when I do this, but he is on the line. And I just wanted to say a closing thanks to Roy Baynes. And he is in front of many of the Phase III trials that really showed incredible monotherapy in combination survival results that really have reshaped the field of oncology.

And I need to point out to many different things. I would just also emphasize it's not just KEYTRUDA, Lynparza, Lenvima oncology, it's also things, for example, like GARDASIL. I know that oftentimes, we think of ourselves as a cancer company, but we should recognize that GARDASIL is a vaccine that essentially reduces the rate of HPV-driven cancers by 90% or so is an incredible tribute to the team, to Roy's team. And I sometimes joke that the path of Merck, as Eric has laid out for the last sort of 10 years, have there's a favorite book that I've had my kids read back in the day, which is Emperor of All Maladies. And essentially, you're going to have to add multiple chapters on the revolution of IO. And what I would say is Roy and his team have rewritten that -- those chapters.

And I just had this pulled out because the chapter, when I say rewritten the chapter, this is the KEYTRUDA label. And this has fundamentally altered every cancer patient, every cancer training program, every hospital throughout the globe. And I just want to give just enormous credit for Roy and Roy would want me to emphasize, it's not just Roy, it's his remarkable team that you've seen here and the remarkable physicians, organization -- the operational organization that has been able to allow us to have this impact.

And with that, I want to leave that to have Peter come up here. But before I go, just Roy, I know you're on the line. I won't embarrass you by asking you to say something right now, but I just want to say on behalf of all of us here, thank you. I know many of the investors here have come to say goodbye to Roy, but unfortunately, Roy is only on -- only available hereby by signing in but not in person. So Roy, thank you very much.

QUESTIONS AND ANSWERS

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

Okay. Thank you very much, Dean. And we're ready to turn it over to Q&A. We have Stephen Domini have mics. Why don't we start with Steve since Steve was the first one here this morning and got the front row seat.

Stephen Michael Scala - *Cowen and Company, LLC, Research Division - MD & Senior Research Analyst*

This is Steve Scala from Cowen and Company. And let me just say thanks to Roy for all your contributions to patient care. So 2 questions. First on vibostolimab lung trials, 2 of the 4 trials still have PFS endpoints. So I'm wondering how Merck is allocating the alpha between OS and PFS in those 2 trials. And why not make the decision now just to drop PFS since it doesn't look like it may get you anywhere?

And then the second question is 2 trials have shown up on clinicaltrials.gov in the last month or so. For Merck, end points or Merck targets, which I don't believe the mechanism has ever been revealed. So maybe you could tell us the mechanism. It's MK-1088 for solid tumors and it's MK-4334 happens to be for schizophrenia.

Dean Y. Li - *Merck & Co., Inc. - Executive VP & President of Merck Research Laboratories*

I'll let Greg to comment on the vibostolimab, especially in relationship to the lung.

Gregory Lubiniecki;VP, Late-Stage Oncology Development^ Thank you, Dean. Happy to do that. So KEYTRUDA is the backbone of the oncology development program or at least a large portion of it. And we've opted to combine vibostolimab with pembrolizumab, KEYTRUDA as part of our development plan. It is true that many of our trials employ the strategy of dual primary endpoints where either PFS or overall survival, if either is positive, then we could declare the study positive. We are reviewing external data related to this pathway as well as looking at our own internal data and applying that appropriately to the design of the clinical studies in question.

Dean Y. Li - *Merck & Co., Inc. - Executive VP & President of Merck Research Laboratories*

Just really quickly, I'd like Eliav to make some comments and then maybe really important to separate the difference between a dual and a co-primary.

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

Yes, I think it's important to understand that there are many ways to manage statistics in a clinical trial. In our circumstance, we have -- one of our secret sauces is our extraordinary biostatistics group that has been able to develop techniques that enable us to apply alpha to different -- in different ways based on emerging data. So I think that the -- there are substantive difference in what we've heard, again, we've not seen the primary protocol for other studies compared to our own. In particular, we're not -- our trials are designed such that one or the other can succeed not if one is negative and the other is negative. So we have to be careful about -- thinking about these trials as individual experiments that have quite different characteristics.

The last thing I would point out is that as we mentioned, as Eric mentioned, our trials are actually designed to look at different populations and those of other compounds. Although, again, we don't have access to the protocols of other combinations. We're pretty confident that we have a very solid way of looking at the effect of adding vibostolimab to pembrolizumab.

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

And the second part of your question, Steve, was 1088. Yes, we might have to get back to you on that. Yes.

Next question, Daina?

Daina Michelle Graybosch - *SVB Securities LLC, Research Division - Senior MD of Immuno-Oncology and Senior Research Analyst*

Two questions for me. One on LAG-3 in Hodgkin's. You put up the PD-1 relapsed/refractory data, and it was exciting. But the PD-1 naive didn't look like it was adding that much over KEYTRUDA. So I wonder what it tells you about the mechanism. And if you'll take that into how you develop Lag-3 and other indications? And my second question is, you highlighted your selective IL-2, which I noticed is in a new clinicaltrials.gov. And I wonder if you could tell us how it's selective and anything else about why you're excited about that approach for IL-2.

Dean Y. Li - *Merck & Co., Inc. - Executive VP & President of Merck Research Laboratories*

So why don't I have Greg take the first one and then Eric, if you could take the second one, that would be great. And I think the first question relates to LAG-3 -- pembro and LAG-3 in hematologic malignancy. And I might even have a question prior to all of this as to what we see past the indications that we have in relationship to heme malignancies for that compound as well. Greg?

Gregory Lubiniecki;VP, Late-Stage Oncology Development^ Thank you. So it is true, and we are very excited about the data that we saw with the favezelimab combined with pembrolizumab in treating patients with relapsed/refractory classical Hodgkin's lymphoma. And you're absolutely right. The refractory setting, as was mentioned here, we saw a response rate around 30%. And these are patients who would have had progression disease within 12 weeks of their last administration of the checkpoint. So seeing a 30% response rate is very impressive.

In terms of the checkpoint naive cohort, there we did see a response rate of around 70%. I will say that this was with a relatively early data cuts. And so we are continuing to watch that data mature and see how that evolves. In addition, though, we are certainly also looking at some other tumor types that have been treated with favezelimab, some non-Hodgkin lymphoma as well as multiple myeloma. And we're waiting to see how those cohorts complete enrollment and seeing how those data mature.

So that at least handles within favezelimab, and then I'll just briefly mention that within the heme malignancy space, just to demonstrate Merck's commitment to trying to advance care in that area, we also are developing nemtabrutinib, which is our non-covalent reversible Bruton tyrosine kinase inhibitor as well as zilovertamab vedotin, which is our ROR1 antibody drug conjugate. The -- nemtabrutinib is -- now that we've identified a dose is being explored in a multi-cohort study of a number of diseases that should be sensitive to that mechanism of action. And our zilovertamab vedotin program has opened up initially in diffuse large B-cell lymphoma with a Phase II study and a large Phase III study and then it's being explored in a number of other non-Hodgkin lymphomas as well.

Eric, on the cytokines and IL-2 specifically?

Eric H. Rubin - *Merck & Co., Inc. - SVP of Global Clinical Oncology & Early-stage Oncology*

Right. So our IL-2 compound is biased towards BT-gamma receptors rather than alpha. So this should improve the therapeutic window of IL-2 targeting and allow development as both a monotherapy and in combination with KEYTRUDA.

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

Great. Next question, please. Terence?

Terence C. Flynn - *Morgan Stanley, Research Division - Equity Analyst*

Terence from Morgan Stanley. You touched on it a little bit your ROR1. You guys obviously have some ADC programs moving along. I think some of the feedback we've heard from physicians at this conference has given some of the maybe less on inspiring IO-IO combo data, maybe ADCs is kind of the way to go particularly for maybe some other solid tumors. So as you guys think about building out your ADC efforts, maybe help us think about how you're thinking about it strategically, internally, externally and where we are in the field?

Dean Y. Li - *Merck & Co., Inc. - Executive VP & President of Merck Research Laboratories*

I'll take a first stab at that really -- that's a good point that you've made, especially in relationship to -- it's the combination of IO with other, what we would call, non-IO mechanisms, whether it be chemotherapy, whether it be ADCs, whether it's with targeted agents, whether this is something that Merck has had a deep interest in. I would just emphasize the advancement of chemo, the advancement of Lenvima and Lynparza is along those lines as well.

In relationship to antibody drug conjugates, we're very interested in antibody drug conjugate. We have a series of partnerships. I think this is public, I'll be corrected later on by Peter, I'm sure. But we have partnerships with Gilead. We have partnerships with Daiichi Sankyo. We have partnerships with Seagen. We clearly have interesting relationship with VelosBio. And we have other internal and other programs as well. So this is a place that we think is really an important pick to keep our attention to.

The other point that I would just emphasize is at least for us, we have a view that the combined ability of medicines is really important. And so that's very important that we're not just interested in the antibody drug conjugate per se, but also what their ability to combine with standard of care, and we happen to have the privilege of having an important standard of care with a PD-1. So I think that becomes an important sort of standard for us to think about it. And as there was a discussion, I think the ability to sort of define not from an academic or theoretical position. But from a real world, how do you actually change the biomarker field that Eric spoke about. We also think that will be critically important as we see that field as advanced. I hope that -- Eliav or Eric or anyone else want to add anything?

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

Great. Thank you, Terence.

Mohit Bansal - *Wells Fargo Securities, LLC, Research Division - Senior Equity Analyst*

Mohit Bansal from Wells Fargo. Two questions from my side. So one on TIGIT. So looking at your trials or in even 1% to 50% EPS in your trial. Could you talk a little bit about the rationale there? Because it looks like in the -- did it seem to work more better in 50% plus, but even that trial did not turn out to be a down positive for PFS? So we'd love to get your thoughts on that.

The second question is regarding in non-small cell lung cancer, pretty much everyone is trying to replace chemo in the chemo-IO combo with either ADC or TKI. So I would love to get your thoughts on -- so I even think that keep chemo is an easy bar to hit. So your thoughts on like what Merck would do to actually have something in combination with KEYTRUDA there because you are the mainstay there. So we'd love to get your thoughts there.

Dean Y. Li - *Merck & Co., Inc. - Executive VP & President of Merck Research Laboratories*

I love that you highlighted that combo chemo is the standard and is a high bar to lay out for any future combination to address, especially in the first line. I think that's an important point that should think in as someone who knows people who have this disease and were faced with those choices. But before I go there, let me just touch really quickly in relationship to the TIGIT sort of question, but I do think you highlight one of the things that I think is important is that our ability, given the broad label, and I don't just mean tumor types, but also biomarker spectrum allows us

to be able to do certain experiments that potentially can't be done by others if you use a different PD-1. And so with that, I just want to make -- Greg, did you want to make any comments specifically?

Gregory Lubiniecki;VP, Late-Stage Oncology Development^ Sure, yes. Thank you. So our non-small lung cancer program is actually quite broad. We'll go specifically -- well, and we believe in having a broad development program. So I'm kind of answering the second one, and I'll go back to the first. But -- so there are multiple combinations that we're exploring. I mean we've demonstrated the benefit of monotherapy, pembrolizumab with survival benefit relative to cytotoxic chemotherapy. And now we've also demonstrated a benefit in combination with chemotherapy. And so we're building upon both the ability to use monotherapy as well as combinations with chemotherapy through a number of different programs.

So there are combinations with lenvatinib, the multi-targeted tyrosine kinase inhibitor. There are combinations with olaparib with olaparib being administered in a maintenance setting. There are, as has been mentioned, collaborations with Daiichi Sankyo using ADCs as well as Gilead. So things are quite broad. In addition, we're always looking for other ways that we can try and develop useful medicines for patients with non-small cell lung cancer.

So specifically, and additionally, as an area of our growth, we're also exploring the use of KEYTRUDA in combination with favezelimab as a co-formulation. And there are studies without chemotherapy as well as with chemotherapy. And it is true that since pembrolizumab, KEYTRUDA does have its label for patients whose tumors have a tumor proportion score of 1% and greater, we are exploring that population in KEYVIBE-003, whereas other companies may need -- or choosing to explore it at 50% and greater, we're exploring at 1% and greater in that trial. And then when we're looking at the co-formulation combination with chemotherapy in combination with chemotherapy, there is an all-comers population in keeping with the label for KEYTRUDA.

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

There's a number of questions on the webcast and many of them involve TIGIT. And I know we addressed it earlier, but I want to make sure we're getting the full expanse of the questions. So Luisa Hector takes it up a notch and elevates just as how have recent competitor data on TIGIT change your view of your own program? And Mara Goldstein from Mizuho says the recent readout of a competitor's anti-TIGIT trial has produced negative results in small cell and non-small cell lung cancer. Can you highlight points of differentiation between your vibostolimab programs, particularly in non-small cell lung cancer? And whether the SKYSCRAPER-02 data and small cell changes your view of that indication?

Dean Y. Li - *Merck & Co., Inc. - Executive VP & President of Merck Research Laboratories*

Let me just put out as a broad statement. I think one thing that I think I've emphasized to this community is pembro is different. It has a broad and just such a wide expansive just in terms of tumor types and its combinability from late to early. When we thought about the IO-IO strategy, whether you're talking about checkpoint inhibitors for T cells, whether you're talking about checkpoint inhibitors for myeloid cells, when you talk about cytokines, it is our view that those combinations will not necessarily have as broad as a sort of breadth and depth that pembro had, that it will be a little bit more bespoke and be a little bit more tumor tissue specific.

So that's why we've invested in a broad portfolio. That's why there are others who, for example, have thrown totally into TIGIT or have thrown totally into LAG-3 or some have thrown totally into cytokines. We believe that it's very important that we have the availability of many of these compounds and especially with Eric's group to be able to interrogate in specific patient populations that becomes important. So I just want to do that as a sort of overview in relationship to that.

In relationship to external and internal data, we have our own internal data. There are differences in the molecules. But to be very honest with you, at the end of the day, the molecules have to show what they do in clinical trials. And so we'll see what those readouts are. But we are informed by the external landscape quite significantly. And I don't know if Greg or Eliav, if you wanted to add anything?

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

Yes, just I would just add that the designs of the clinical trials are not the same across the board, and there's meaningful differences between them in each of the studies, in each of these settings. The questions about, for example, the 1% to 49% show that -- in that context because pembrolizumab is uniquely potent and has a very broad usability and history in that population. We're able to see where their incremental benefits can be observed in a situation where maybe PD-1 levels are not quite as high, or PD-L1 level is not quite as high. So I think that there's -- there we have a unique capability to interrogate the breadth and depth of the lung cancer field, given the history that we've had with pembrolizumab.

Obviously, the clinical trials have to do -- have to show us that early data are only indicative or directional or give us some initial impetus to take it forward to Phase III. And as Dean noted, we'll see what the Phase III trial show. But I'm very confident that our trials are designed to investigate this combination in a consistent way across a broad spectrum of diseases based on a very deep knowledge of lung cancer, particularly immunotherapy in lung cancer that really Greg and his team have been able to provide to us uniquely over the past few years to establish pembrolizumab as the basis for treatment of advanced and metastatic lung cancer.

Dean Y. Li - *Merck & Co., Inc. - Executive VP & President of Merck Research Laboratories*

And I would just add that our design of KEYVIBE-003 is based on our own data, looking at the combination of KEYTRUDA and vibostolimab, where there has been an increase in the response rate for patients from 100% on the TPS scale.

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

Great. Chris?

Chris Shibutani - *Goldman Sachs Group, Inc., Research Division - Research Analyst*

Chris Shibutani from Goldman Sachs. Two questions for KEYTRUDA in the adjuvant lung setting, 091. Can you provide us an update on the 50% plus and high subgroup, your confidence in terms of any regulatory considerations and dialogue for that ultimate adjuvant indication?

Secondly, with the TIGIT program, KEYVIBE that you outlined here, the Phase III studies, quite a few with primary completion dates in the 2025 and beyond period. Can you comment if there's any opportunity for interim analysis or incremental insights prior to that time frame?

Dean Y. Li - *Merck & Co., Inc. - Executive VP & President of Merck Research Laboratories*

Let me just give it to Greg to just talk briefly about KEYTRUDA lung adjuvant in relationship to KEYNOTE-091. If you don't mind, I'd also -- because there's been other questions that come up, I'd love Scot to just talk more broadly about adjuvant and other indications, which we think is critically important. And then we can come back to Eliav about abilities to see interim analysis for some of these trials and what the timing is. So Greg, Scot and then Eliav?

Gregory Lubiniecki;VP, Late-Stage Oncology Development^ Thank you. So KEYNOTE-091 is a study of patients who have non-small cell lung cancer, Stage Ib to IIIa. After their tumor has been completely resected, then they were randomized to receive either placebo or pembrolizumab as part of their adjuvant treatment regimen. And at the second interim analysis for the study, it was identified that there was a 24% reduction in disease-free survival for those patients who had pembrolizumab as part of that adjuvant regimen relative to those who did not. And that was observed irrespective of PD-L1 expression and across all those stages that were included in the study. And so therefore, we have great confidence that this pembrolizumab is providing benefit to all the patients who receive it.

In terms of the regulatory question, I'm not able to comment at this time on our regulatory interaction.

Dean Y. Li - *Merck & Co., Inc. - Executive VP & President of Merck Research Laboratories*

Scot, if you want to talk about...

Scot Ebbinghaus;VP, Late-Stage Oncology Development^ No, I think to try to put KEYNOTE-091 into a little bit broader context, it's important to remember that KEYTRUDA was first approved in an adjuvant setting several years ago. Now in Stage III melanoma. And we've really laid out a very careful development program in early disease states across a broad number of malignancies. We have very nicely outlined the contribution of data that we had at this particular ASCO, which was demonstrating the distant metastasis-free survival benefit of KEYTRUDA in stage II melanoma as well as in renal cell carcinoma.

We didn't talk at all or talk much about KEYNOTE-522, but that's another example of integrating pembrolizumab into earlier disease states. And then I think the other important thing is that we have roughly 20 pivotal trials ongoing. They have around 20,000 patients in them that will further elucidate the value of pembrolizumab in early disease states. That's a really robust program and one that we're quite proud of and quite anxious to see continue to read out as with KEYNOTE-091.

Dean Y. Li - *Merck & Co., Inc. - Executive VP & President of Merck Research Laboratories*

Eliav?

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

Yes. The question had been about readouts. And obviously, we have a series of interim analysis that we have. But I think the base case is that we would have readouts between '24 and '26, 2024 and 2026 for many of these studies. We want to make sure that we have a definitive answer to questions. Obviously, as data progress and if there are events that are meaningful, we would share those as we can.

I'd also point out with KEYNOTE-091 that, that study continues and we will continue to have further information that will be relevant to treaters and to regulators. And we also have our neoadjuvant-adjuvant trial, KEYNOTE-671 that will be reading out in due course.

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

Great. Thank you. Seamus?

Seamus Christopher Fernandez - *Guggenheim Securities, LLC, Research Division - Senior Analyst of Global Pharmaceuticals*

Seamus Fernandez, Guggenheim Securities. So just a couple of quick questions. First, can you guys comment on your view on access to AstraZeneca's PARP 1? I think some of those data look interesting and there's a little bit of controversy, I think, around that, whether or not you can access the PARP 1 as part of that collaboration.

The second question is just as you look across all of the collaborations, research collaborations that you've run, Merck established many times in conversations that you expected to have quite a bit more information to get better access to products on a go-forward basis. And I think really the only product where we've seen unique benefit in combination with KEYTRUDA is either chemotherapy or PAD set. So just trying to get a better understanding of when you feel we'll start to see emergence of new clinical mechanisms or chemotherapy really is whether delivered by an ADC, the ideal combination agent for KEYTRUDA?

Dean Y. Li - *Merck & Co., Inc. - Executive VP & President of Merck Research Laboratories*

Let me take some of those and then I may send it back down to maybe Eric or Scot, as I think through this. In relationship to PARP, I think the PARP story is an important story. We've had a great working relationship with AZ in relationship to it. I would just emphasize, when I think about PARP was there focused on a biomarker-specific block, then it got extended to HRD as Eric highlighted. And we're going to -- we are exploring in our clinical trials what is the importance of PARP outside of those biomarkers, especially in some of the key links I just discussed. So I think that will steer us to how important a combination and how to think about DNA recombination or repair is.

In relationship to our collaboration with AZ, we've had a strong collaboration in PARP inhibition. And I think at a later time, we'll have a more fulsome discussion, but we look forward to continuing to work with them on Lynparza and PARP more generally as well.

In relationship to your question about combinations, I just want to sort of -- yes, it is. You've asked about PARP, you've also talked about chemo. But I just want to emphasize that, for example, the readouts that we have with, for example, Lenvima tells you something about maybe what the role is with angiogenesis. I'll just really quickly just ask, for example, Scot and Eric to make comments about that. But when you see wherever angiogenesis has a signal and there's a movement in that and potentially in relationship to KEYTRUDA, you start asking yourself what are other modes to affect angiogenesis. And I think, for example, Scot can speak about how he thinks about belzutifan as when you think about HIF-2 alpha or you think about HIF, you often think about angiogenesis. So that driving of how you lay out your pipeline, both internally and externally, I think are in display with that.

But just quickly, Scot, did you want to mention anything in relationship to how you think about angiogenesis and Lenvima? And how that might inform you about other compounds, for example, belzutifan or something like that as a weighting out to your question?

Scot Ebbinghaus;VP, Late-Stage Oncology Development^ I think you've made a very good point, Dean, that we've had really, I think, quite tremendous success with the KEYTRUDA plus Lenvima program, renal cell cancer being a great example. And of course, renal cell cancer is sort of the poster child of an angiogenic tumor phenotype, where VEGF kinase inhibitors have been sort of the cornerstone of therapy for many years and they combine very, very well with pembrolizumab.

If you think about HIF-2 alpha, it's actually just upstream of VEGF and so it's sort of logical that, that is going to be critical in particularly renal cell cancer, where there's a high rate of VHL loss even in the sporadic disease setting. But perhaps even in other tumor types where angiogenesis is a critical component of the tumor genesis or the tumor pathway, and so we're investigating KEYTRUDA, Lenvima and belzutifan in combinations in certain GI tumors, for example, where angiogenesis is critically important to the pathogenesis of the disease.

Dean Y. Li - *Merck & Co., Inc. - Executive VP & President of Merck Research Laboratories*

I'll just ask Eric to just make comment especially in relation to PARP and this concept of biomarkers, BRCA, HRD, HRRm and also the importance of seeing how combinations can often sort of broaden and even pass in a biomarker agnostic way. Eric?

Eric H. Rubin - *Merck & Co., Inc. - SVP of Global Clinical Oncology & Early-stage Oncology*

Yes. I mean I'll just take one step back because I think it's an important question. I think you probably have the broadest combination strategy for KEYTRUDA. In part, this comes from our external collaborations group, where we're partnered with many companies, more than 100 trials involving very diverse mechanisms. And I think while we have great basic scientists that have used, for example, post-treatment biopsies in patients who've gotten KEYTRUDA to try to understand mechanisms of resistance and new targets, and those have led to things like our myeloid targeting programs with ILT3 and ILT4.

We recognize that we -- sometimes those models aren't all that predicted. And so we -- again, a very diverse combination program that span IO combinations. Chemotherapy, you mentioned, I think in the early days, people were skeptical whether that would work. And in fact, it's quite effective. As you know, we have combinations with personalized cancer vaccines, KRAS, cytokines, very broad and we're seeking to find the most active combinations by really studying them in the clinic in small groups of patients looking for large signals.

And yes, I think in some cases, of course, we're always pursuing biomarkers for each of those to try to identify potential diagnostics that could further increase the effect size for the combinations.

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

Great. Thanks. We're running a little short on time, but I know I want to get to as many questions as possible. There's a few more on webcast. One related to Seamus' question on combos. Chris Schott asked, can you talk about the tolerability of your CTLA-4 as we think about the triple combo you are developing in renal with KEYTRUDA and Lenvima?

Dean Y. Li - *Merck & Co., Inc. - Executive VP & President of Merck Research Laboratories*

Yes. So combinatory and tolerability is always, I think, really important relationship with combo. Eric or should -- Eric is that -- and then Scot.

Eric H. Rubin - *Merck & Co., Inc. - SVP of Global Clinical Oncology & Early-stage Oncology*

Yes, so we very carefully developed our anti-CTLA-4 and careful dose-finding studies, in particular, looking at the dose in combination with KEYTRUDA. It's clear that for CTLA-4, dose optimization for monotherapy in combination with anti-PD-1 is different. So we have a dose that's 25 milligrams is our recommended dose, and it combines well with KEYTRUDA with a safety profile that's perhaps better than observed in other combinations where the dose is higher. And so it does lead to a tolerable combination as well with triplets such as with Lenvima.

Dean Y. Li - *Merck & Co., Inc. - Executive VP & President of Merck Research Laboratories*

Scot?

Scot Ebbinghaus;VP, Late-Stage Oncology Development^ And I was just going to add that we've got the triple combo in one Phase III study in renal cell cancer as well as in an open-label study in hepatocellular. And I would say that the tolerability of the triplet is unlikely to be a concern or a problem at this point.

Dean Y. Li - *Merck & Co., Inc. - Executive VP & President of Merck Research Laboratories*

I just want to, yes, emphasize the point that Eric and Scot made about specific programs. But this issue of combinability, I think, is really important. It's something that we take seriously, both in the design of the molecules and the preclinical development and clearly the clinical. And that's true in relationship to what the question was specifically with IO-IO, but I would also emphasize the same thing will be true for chemo, for antibody drug conjugate. I would also emphasize that for RAAS inhibitors will be very important in relationship to that. And again, we've talked about PARPs and such. So I do think oncology is a place where there's lots of combinations and sequencing and those considerations will be really important.

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

Another common question. Tim Anderson from Wolfe. Can you talk about whether it is better to give LAG-3 and PD-1 as a bispecific like Roche is doing? Roche claims it is more targeted that way with less immunosuppression. What are Merck's thoughts on their early data?

Dean Y. Li - *Merck & Co., Inc. - Executive VP & President of Merck Research Laboratories*

I will let Eric answer this one because there's always this question of how you think about putting a bispecific and what a bispecific does versus having 2 things added together. And there's a complexity and relationship to PK/PD, but there's also a basic biology question that comes with that. Did you want to...

Eric H. Rubin - *Merck & Co., Inc. - SVP of Global Clinical Oncology & Early-stage Oncology*

Again, I think it really has to test in the clinic, right? So we have clinical data with our LAG-3 combination that looks impressive and sufficiently impressive that we've taken it to Phase III in both microsatellite stable colon cancer as well as PD-1 progressed lymphoma. So again, the data sort of speak for themselves.

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

Great. Maybe final questions. I see one last hand up in going there.

Evan David Seigerman - *BMO Capital Markets Equity Research - MD & Senior BioPharma Research Analyst*

Evan Seigerman from BMO. Sorry for my voice, it's allergies, not COVID. So I wanted to touch on MK, what is the 1084, your KRAS G12C. Can you discuss or provide some color as to what differentiates this asset from sotorasib and adagrasib where we've gotten lots of data at recent medical meetings, including this one? And just given your Phase I trial design, how could you potentially accelerate development of this asset to, say, catch up to sotorasib or adagrasib?

Dean Y. Li - *Merck & Co., Inc. - Executive VP & President of Merck Research Laboratories*

Eric, did you want to take a shot at that and then I can answer some questions?

Eric H. Rubin - *Merck & Co., Inc. - SVP of Global Clinical Oncology & Early-stage Oncology*

Yes. I think we've designed a very potent molecule that we do think has the potential to differentiate. Of course, again, we've got KEYTRUDA as the backbone. And I think our -- we have a lot of experience in designing efficient Phase I clinical trials. And so we're working to quickly get to a dose as both a monotherapy and in combination with KEYTRUDA in that study.

Dean Y. Li - *Merck & Co., Inc. - Executive VP & President of Merck Research Laboratories*

Yes. I mean just from a broader sort of standpoint, I think when you have a covalent inhibitor, which is essentially a reactive molecule, having a potent molecule so that you don't have to put a whole bunch of that molecule in, will create a possibility -- theoretical possibility of you being able to dose it with not as much potential half target, and it may be really important in combinations. If you have a program where you don't have to reduce the dose of what you saw in monotherapy and combination, that would be really important. But those are the sort of -- that -- I come from the discovery and where we think about that. But having said that, at the end of the day, you have to play it out.

The other sort of thing is I would just emphasize the game is initially G12C, but that's all recognized. There are other ways to do it. There's also G12D. There's other mutations that will be really important. There is the possibility of thinking about from a pan-KRAS standpoint, how to address that. And so there's a lot of opportunity there as well as combinations, not just in relationship to PD-1 or something like this, but also other pathways. Some people talk in terms of shift, some people talk about that. So we think it's a great advancement since that 2013 paper, but I think there's a lot of game play in relationship to KRAS and RAP more generally moving forward.

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

Thank you, Evan. And thank you all for coming out early on Tuesday of ASCO. We appreciate your live attendance, and thank you to all that tuned in via the webcast. And apologies to those of you that I didn't get to your questions, please follow up with IR and we'll try to get responses to you. We look forward to staying in touch. Dean, any final comments?

Dean Y. Li - *Merck & Co., Inc. - Executive VP & President of Merck Research Laboratories*

No, I would just -- the final comment is we were so happy to meet in person. I hope this was a useful update of looking at a year ago, where we were, where we are now and we hope to continue to do this in the future. I think you've also seen that, that the ability for us to really make this impact on oncology is a legacy of great leadership that is laid out here, but a great leadership that was laid out here that was trained and mentored by Roy Baynes who is online as well and someone that I know that many of us and many of you had wished was here to offer thanks for what he has done for the field. Thank you very much.

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

Thank you.