REFINITIV STREETEVENTS

EDITED TRANSCRIPT

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PRESENTATION

Operator

Welcome to the Merck & Co., Inc. investor event at the American Society of Clinical Oncology annual meeting. (Operator Instructions) This call is being recorded. If you have any objections, you may disconnect at this time.

I would now like to turn the call over to Mr. Peter Dannenbaum, Vice President and Investor Relations of Merck. Sir, you may begin.

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

Thank you, Holly, and good evening, everyone. Welcome to Merck's investor event here at the American Society of Clinical Oncology annual meeting. Thank you to all of you who have made the effort to be here with us live, and thank you to everyone tuning in via the webcast. We're obviously very excited to have this opportunity to speak to you about Merck's oncology program.

During today's call, a slide presentation will accompany our speakers' prepared remarks. It's been posted to the Investor Relations section of our website. And before we get started, we'd like to remind you that some of the statements that we make during today's call may be considered forward-looking statements within the meaning of the safe harbor provision of the U.S. Private Securities Litigation Reform Act of 1995. Such

statements are made based on the current beliefs of Merck's management and are subject to significant risks and uncertainties. If our underlying assumptions prove inaccurate or uncertainties materialize, actual results may differ materially from those set forth in the forward-looking statements. Please reference this slide in our presentation and our 2022 10-K, which identify certain risk factors and cautionary statements.

I would now like to introduce Dr. Dean Li, President, Merck Research Labs, who will make a few opening remarks and outline our agenda and speaker lineup. Dean?

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

Thank you, Peter, and it's great to see many of you who we met last year. And I think I would take a few moments to provide a little context and introduce this evening's event. First, we will have Eliav Barr, who will provide an update on our oncology strategy and development program and the progress we continue to make. It has been a little over year since Eliav transitioned into his role as Head of Global Clinical Development and Chief Medical Officer. And in that short time, we have made tangible progress as evidenced not only by the data presented at this year's conference, but also the advancements across our oncology pipeline and our ability to augment our pipeline through strategic business development transactions, some of which we will touch upon today.

Next, Greg Lubiniecki, Vice President of Late Oncology Development, will provide an overview of our earlier-stage lung cancer program, including the remarkable data we presented for KEYNOTE-671. Now Greg has been playing an instrumental role in steering all of our lung cancer program through key milestones, including the pioneering KEYNOTE-189 study of KEYTRUDA in combination with chemotherapy for metastatic lung disease, to present day as we seek to build upon our learnings and treat patients at earlier stages of lung disease or lung cancer.

Following Greg, I am pleased to welcome Marjorie Green. Marjorie recently joined our global clinical development team as Senior Vice President and Head of late-stage oncology. She comes to us from Seagen, where she was Senior Vice President and Head of Late-stage Oncology, leading the clinical development of a diverse portfolio of oncology candidates, including multiple antibody drug conjugates. Of note, Marjorie played a pivotal role in the recent approval of KEYTRUDA and PADCEV in urothelial cancer.

These results provide the first evidence of the combinatorial benefit of an ADC and a checkpoint inhibitor in these patients. Prior to Seagen, she spent time at Genentech, and we are excited to have her join us today and provide an overview of 4 of our novel candidates entering Phase III trials this year.

And importantly, in this setting, Chirfi Guindo, our Chief Marketing Officer, will round it out with an update on the commercial landscape and our ability to further impact the lives of patients and their families. I will then provide closing remarks before we open it up to Q&A. So we've assembled a stellar lineup for all of you for today's event. And without further ado, I will turn it over to Eliav to kick us off.

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

Great. Well, it's a real pleasure to be with you. I know this has been a pretty long congress, and we're all exhausted. So I hope we'll -- you'll enjoy this update that we'll have on our oncology pipeline, which I'm really super excited about.

So we have a really robust portfolio. It's an extraordinary move from a world where we were once just KEYTRUDA or KEYTRUDA and a couple of friends, to a multipolar pipeline that includes a tremendous number of exciting candidates. KEYTRUDA really laid the foundation for improving outcomes in patients with cancer, but we all know that there's plenty of room to go to try to make cancer into a chronic disease or a curable disease.

So we've got about over 20 different items -- drugs in our portfolio. And we can divide them into 3 segments. The first segment is those that boost the anti-tumor immune responses. Those -- and then there's those that are designed to increase cancer cell sensitivity to tumor-killing drugs, and those designed to impact pathways that drive cancer growth.

Now if we look at the immune booster category in the first column there on your left, we're developing combinations of pembro with a variety of different products, including TIGIT, which where we've had the heaviest investment, as you probably know. We're particularly excited with our collaboration with our partner, Moderna, where we're evaluating the addition of individualized neoantigen therapy to pembrolizumab to see whether we can improve outcomes, particularly in early settings. And I think I hope you've seen some of the data that were presented earlier in this congress.

In the tumor-targeting category right there in the middle, we've gained access to a variety of really high-quality antibody drug conjugates and immune engagers, of which MK-2870 is the most advanced and 2 others have now entered the clinic, and we look forward to presenting them in due course. I hope you've seen the poster for MK-2870 that was shown at this meeting, and I look forward to sharing even more information about it as the data roll out.

So finally, all the way at the other end of the slide, we have our precision medicines, and those are -- include things like belzitufan, our HIF-2-alpha inhibitor; MK-5684, our CYP11A1 inhibitor for prostate cancer; and bomedemstat, which is our LSD1 inhibitor. And you'll hear about some of these later on in the presentation.

And all of this is underpinned by our pretty excellent discovery pipeline in earlier phases of development that give us the confidence that we're going to be able to continue to build on our leadership position in oncology and build new and differentiated molecules that will improve and push the needle on outcomes.

Now we follow a structured kind of approach, which is establish, expand and extend approach when we're thinking about advancing notable candidates for cancer [litho] promise. And we followed this approach for KEYTRUDA over the years. And now we're beginning to establish our beachhead first indications for a variety of ADCs and precision medicine targets. And you'll see that over the course of the next few months as clinicaltrials.gov becomes particularly active for our oncology portfolio. We plan on initiating quite a few Phase III trials, and we look forward to being able to share the rationale behind those trials with you in due course.

We're also working to expand to the tumors, where there's a need for new options for patients and attempting to deepen those responses that we've seen in our approved indications for pembrolizumab. And here, having pembrolizumab as a foundation provides us with a real competitive advantage. It's an advantage both in terms of placement in the field. But also, it allows us to refer back at a more coherent way, in a more detailed way to our clinical database to make proper bets, proper study designs and proper prioritization decisions. So we plan a rich set of studies that will evaluate combinations within categories, across categories that might include things like IO plus IO, might include IO plus precision medicines, or as we now are able to do, ADC plus ADC.

And of course, we're extending the use of our medicines beyond the later stage of disease with a focus of early disease settings. Now of course, the idea here is, as you all know, the earlier you diagnose cancer, the more likely you are to achieve long-term remission or to dare for a cure. And we want to be able to provide viable options earlier in the diagnosis to do that. And I think KEYNOTE-671 provides kind of the standard for the lung cancer field. And it follows the same approach that we've chosen for KEYNOTE-522, which is really revolutionized how triple-negative breast cancer is treated in the operable setting.

We also aspire for cancer prevention. And I think we'd be remiss not to note that the American Cancer Society's annual report on cancer effects and trend have noted that the observation that there's been a 65% reduction in cervical cancer incidents in women 20 to 24 years of age over the past few years. And you know that, that benefit has come because a variety of things, the majority of which is GARDASIL-9 and our ability to prevent certain anogenital and HPV-related cancers.

I think that this is something fantastic and will continue to be a source of great public health benefit and, consequently, will be very meaningful for Merck over the course of the next years as we build and extend the GARDASIL franchise to other cancers, including the head and neck cancer area.

Now as I look at all of this, the way we've structured our portfolio is to think about how we attack each stage of cancer and each kind of cancer. And so we have a breadth of studies across different stages of disease. And in the inoperable or metastatic settings, which you show here, we're

evaluating combinations of pembro with a broad range of agents, both from the pipeline that I just showed as well as external collaborations with a variety of partnerships. And we've had literally hundreds and hundreds of collaborations that have enabled us to have unique insights to understand how you can combine pembrolizumab with a variety of agents in what setting and what kind of biomarker-defined populations. And I think that's been a very important part of the way in which we structured our portfolio as well as our choices around clinical trials.

An example of that is the work to combine pembro with enfortumab vedotin and/or PADCEV for treatment of some patients -- certain patients with advanced or metastatic urothelial cancer who are ineligible for cisplatin. And this is the first indication for a combination of an IO agent and an ADC. So we have to keep that in mind. This is a really exciting moment. We strongly believe that this is going to be the first of the whole plethora of I-O plus ADC combinations that will help patients.

In the metastatic setting, MK-2870 is our current star, and we've shown at this meeting that ADC is very active across a variety of tumor types with no serious ILD to date in a very high-quality clinical program that's going to come forward. Again, leveraging our leadership position with pembro and our ability to gain unique insights based on the same kinds of science has led us to develop KEYNOTE-671, which I think is going to be such an important milestone for early-stage lung cancer.

We've also chosen to increase our focus in hematology through our acquisition of bomedemstat, and you'll hear about that a little bit and how we're going to use that drug for myeloproliferative neoplasms. So I think this is a pretty big effort in the kind of the advanced metastatic setting.

Now several years ago, we initiated a whole bunch of studies of pembro in early cancer. And again, as I mentioned, early cancer is an attractive opportunity at an attractive way in which can reduce cancer risk or cancer death because we can achieve a potential cure or long-term remission. Those studies take a long time to start and get going because we're looking at harder end points and end points that occur less frequently as we are thinking about things like recurrence. And we've already shown throughout here, and you can see the different colors, settings where KEYTRUDA or separately LYNPARZA has been able to be active in early-stage cancers. And we have a total of 8 approvals so far. And KEYNOTE-671, as you recall, has already been accepted by FDA for review.

We're well into the review process, and we are looking forward to hopefully being able to get it out for use by the broader population of patients in the United States later on this year. And we'll talk a little bit more about why we're so excited about 671 a little bit. We've got more than 25 or so active Phase III trials in this early stage of cancer. We're going to focus our attention going forward, and you'll see clinicaltrial.gov lights up with a multitude of Merck studies that we plan on being able to continue in advance on the platform of exciting results, such as KEYNOTE-522, such as KEYNOTE-671, KEYNOTE-091 to bring forward drugs as diverse as our INT therapy and our ADCs. So we really hope that we'll be able to make an impact for patients with cancer in that way.

Now as we move to earlier stage cancers, I think it's important to recognize that we want to be able to extend patient benefit through added innovation. And some of that innovation is not about a new molecule with a new MK number or something like that, but the development of approaches that can help patients maintain their normal lives. And this is particularly important in the early cancer settings where most people are still working, most people are young, most people want to have a regular life. And our job is to be able to extend their lives, improve their outcomes and do so in a manner that doesn't require them to take long chunks of time away to be in a cancer center.

So we prioritized the use of our subcutaneous pembrolizumab program, which is displayed here with hyaluronidase with that particular purpose in mind. So what we want to be able to do is to have something that's available for q3 week or q6 week dosing. The q6 dosing, as you can imagine, especially if that's the only drug that people are using, the adjuvant setting is very attractive, 1 injection over a few minutes, every 6 weeks, you're in and out, and off you go. The hyaluronidase, in our point of view and what we've seen, is that it really improves the dispersion of the drug in -- the skin. It reduces in duration, skin reactions and enables us to inject a little bit faster than we would otherwise have been able to do.

So again, we're looking at this as an innovation that might not be a new molecule but will be really meaningful for patients and health care systems that can obviously have less patients and chairs. And frankly, the younger and people with curable disease, the last thing they want to see is someone across the clinic who's in a metastatic setting that's just is a pretty big downer for them, I'm sure. So we're really excited about that as well.

Now last but not least, we really remain steadfast in our commitment to biomarker research and to identify those patients who will most likely respond to therapy. For us, we've been able to use this notion of biomarker-defined populations to make meaningful changes in the way in which people think about cancer. And I think the MSI high and TMB high indications that we've had for pembro have been really, really important. We really also are focusing our attention on how to use biomarkers now that we have this gargantuan pipeline that's really exciting with a buffet of amazing opportunities probably better than the dinner that you're having here. But anyway -- and we're looking forward to enhancing precision medicine tools and to being able to use the kind of work that we've done to bring forward by market defined populations throughout the KEYTRUDA program and being able to apply that to our ADCs, particularly, but also to other medicines.

And we have a pretty good track record about this, with this 20 biomarker derivative indications. And of course, on the right side, a whole bunch of the potential suspects that we might be able to address. Not only do we -- are we looking at biomarkers for these, we're also, of course, have medicines that might work to silence some of these tumor drivers and so on.

So very exciting time in Merck Oncology. It's a time when we're moving from -- we told you that we were going to move to a new era. The team that's done oncology at Merck wrote the book on I-O. And now we're ready to write Chapter 2, and we're already beginning the authoring process.

So with that, I'll turn it over to Greg to tell us about KEYNOTE-671 in early cancer.

Gregory Lubiniecki - *Merck & Co., Inc. - VP of Late-Stage Oncology Development*

Thank you very much, Eliav. Good evening, everyone. So it's going to be my pleasure to review our early-stage thoracic development program with you. So as you are well aware, patients with early-stage cancers are in the fortunate position of having an opportunity for cure. Usually, the earlier the stage, the better the outcome that patients may have with treatment. Unfortunately, surgery or radiation alone for Stage II or III non-small cell lung cancer needs some assistance to improve patient outcomes. Those who are able to receive adjuvant chemotherapy after the surgery and then adjuvant checkpoint inhibitor will have some benefit, but those patients may still relapse. So there's considerable room for us to try and do better.

Merck has invested substantially in improving treatments for early-stage lung cancer. You can see 2 studies here on the far left of the screen are for patients who are going to use surgery as their definitive modality of treatment. And then the other 4 studies here on this slide are examining the use of pembrolizumab in combination with radiation therapy.

Three of these studies will look at the use of cytotoxic chemotherapy with the radiation. And one of these studies is -- while most of them are in non-small cell lung cancer, one of them is in limited stage small cell lung cancer, KEYLYNK-013.

KEYNOTE-671 is a special study in early-stage non-small cell lung cancer because it modifies the standard way that we have treated Stage II or III in non-small cell lung cancer. Typically, that has been with the use of adjuvant or neoadjuvant cytotoxic chemotherapy. This, however, is -- KEYNOTE-671 is a paradigm-shifting strategy for the treatment of non-small cell lung cancer. KEYNOTE-671 evaluated the administration of chemotherapy and pembrolizumab before surgery for 4 cycles, followed by up to a year of adjuvant pembrolizumab.

KEYNOTE-091, a more traditional treatment paradigm, was able to demonstrate that after surgery, the use of adjuvant pembrolizumab after adjuvant chemotherapy can reduce the risk of the disease recurring or patients dying from disease. However, here, in KEYNOTE-671, we see an even greater risk reduction by 42% in that time-to-disease recurrence or a patient's risk of death when pembrolizumab was administered both before and after surgery with the neoadjuvant chemotherapy.

Of note, these benefits were observed irrespective of age, PD-L1 status, histology. All subgroups benefited from the treatment.

We also observed that a trend towards benefit in overall survival was observed. And that's remarkable given that the median follow-up study on this time is only at 25 months.

Importantly, an exploratory analysis revealed that patients were benefiting from receiving pembrolizumab before surgery and after surgery irrespective of whether all the tumor cells were dead at the time of surgery, or if some tumor cells were still alive at the time of resection. These data are unique relative to what has been published already in the literature. And this is a distinguishing feature of this study and suggest the importance of incorporating both neoadjuvant and adjuvant pembrolizumab to treat early-stage non-small cell lung cancer.

Pembrolizumab is the only checkpoint inhibitor that has shown an improved outcome in 2 ways of treating early-stage, non-small cell lung cancer. One, through the more traditional adjuvant treatment paradigm; and secondly, through this more innovative treatment paradigm where checkpoint can be given neoadjuvantly and adjuvantly.

With that, I thank you, and I'm going to turn the baton over to Marjorie, who is going to discuss some of our exciting compounds in the pipeline.

Marjorie Green - *Merck & Co., Inc. - SVP Late Stage Oncology Development*

Thanks, Greg, and good evening, everybody. It's great to be here with you, and I'm honored to be part of Merck's talented team. Merck has demonstrated excellence in innovation and science, clinical strategy and study execution. It's an exciting time at Merck. We have a promising portfolio and expanding pipeline of oncology candidates. I look forward to helping extend our leadership and improve outcomes for people living with cancer.

As Eliav highlighted, we have a broad program of new agents with novel mechanisms that are advancing across multiple tumor types. In addition to progressing our internal programs, we have made meaningful progress augmenting our pipeline with science-driven business development. Today, we're going to talk about 4 molecules that we've accessed through business development last year that are entering Phase III studies in 2023. These include MK-2870; TROP2 ADC, which Eliav talked about earlier, in collaboration with Kelun; V940, an individualized neoantigen therapy in collaboration with Moderna; MK-5684, which is a CYP11A1 inhibitor, which is being done in collaboration with ORION; and then bomedemstat, an LSD1 inhibitor which we brought in through the acquisition of Imago.

Here, at Merck we're a leader in advancing the science of immuno-oncology and have proven the benefit of pembrolizumab in combination with chemotherapy.

ADC, I geek out about ADCs. ADCs represent the next generation of tissue-targeting chemotherapy by delivering potent anticancer agents directly to the tumor site. Earlier this year, we did receive accelerated approval for KEYTRUDA in combination with PADCEV for treatment for certain patients, who have locally advanced or metastatic urothelial carcinoma who are not eligible for a spot in chemotherapy. This marks the first time KEYTRUDA has an approval with an ADC, and I think this is the first of many to follow. We look forward to building on the success with our portfolio of ADC candidates.

Through our collaboration with Kelun, we are accelerating our pipeline of ADCs by adding 9 candidates in various stages of development and are being evaluated both as monotherapy and in combination with other agents. The furthest along of these 9 is MK-2870, a TROP-2 ADC, which we were studying in a range of solid tumors, including non-small cell lung cancer, which I'll provide more details about in the next slide. Beyond MK-2870, we have 2 additional clinical ADCs, one of which advanced the clinic earlier this year, and 6 clinic-ready ADCs, each with different targets. We expect to share more information about these ADCs in the coming months.

As I mentioned, MK-2870 is our TROP2 ADC. We believe this has the potential to benefit patients across multiple tumor types and across multiple lines of therapy. MK-2870 demonstrated encouraging antitumor activity in a Phase I/II study for patients with relapsed or refractory locally advanced metastatic non-small cell lung cancer. Of the 39 patients treated in the study, 44% achieved an objective response with a median duration of response of 9.3 months. And the patients whose tumors have an EGFR mutation, an objective response rate was seen in 60% of patients with a median progression-free survival of 11.1 months. All of these patients had progression despite prior EGFR TKI therapy, and 50% of these patients had also received at least 1 chemotherapy regimen.

Importantly, for the totality of the patients enrolled into the study, antitumor activity was observed regardless of TROP2 expression level. MK-2870 has a manageable safety profile. There is no evidence of interstitial lung disease or any adverse event treatment-related discontinuation. Based

upon the encouraging data as well as data from other ongoing trials, we will initiate a global Phase III program for MK-2870 in non-small cell lung cancer as well as additional tumor types.

In collaboration with our partner, Moderna, we presented distant metastasis-free survival results in the Phase II KEYNOTE-942 trial. This study evaluates investigational individualized neoadjuvant therapy in combination with KEYTRUDA in patients who have Stage III or IV melanoma following complete resection. Distant metastasis-free survival is a key secondary endpoint of the study. And the overall intention to treat population, adjuvant therapy with V940, in combination with, KEYTRUDA reduce the risk of developing distant metastasis or death by 65% when compared with KEYTRUDA alone. These results build upon the very promising 44% improvement in recurrence-free survival which is the study's primary endpoint that was presented at the AACR meeting in April.

Based upon the data from KEYNOTE-942, the FDA and EMA granted breakthrough therapy designation and prime scheme, respectively, for V940 in combination with KEYTRUDA for the adjuvant treatment of patients with Stage III/IV melanoma, following complete resection. With an existing foundation of KEYTRUDA in earlier stage disease across multiple tumor types, we can clearly evaluate the benefit of combining V940 with KEYTRUDA. We look forward to working with Moderna to initiate a Phase III study for adjuvant treatment of melanoma this year.

Next, I'd like to highlight MK-5684, which is a novel CYP11A1 inhibitor. We are codeveloping this with Orion for treatment in metastatic castration-resistant prostate cancer. Globally, prostate cancer is the second most common cancer in people assigned male at birth. Metastatic castration-resistant prostate cancer is a disease with a particularly poor prognosis, and it continues to be an area of high unmet need. Newer second-generation anti-hormonal agent, such as abiraterone, inhibit CYP-17. Evidence, however, has shown that tumors can actually continue to be stimulated by testosterone as CYP-17 inhibition does not provide complete chemical castration.

CYP11A1 acts upstream of CYP-17, so you can't get the steroid hormones going down to CYP-17. And so by targeting CYP11A1, MK-5684 provides a compelling approach suppressing the synthesis of all steroid hormones and could, therefore, be beneficial in this patient population. This agent has demonstrated promising antitumor activity and a manageable safety profile as monotherapy and people who have heavily pretreated metastatic castration-resistant prostate cancer. And the Phase II portion of the CYP trial, 53% of patients achieved a serum prostate-specific antigen reduction of at least 50% from the baseline concentration. These are patients, who had received prior newer anti-hormonal therapies. In collaboration with Orion, we look forward to advancing this agent into Phase III development this year.

Finally, moving into hematology, bomedemstat is a potentially first-in-class, orally available lysine-specific demethylase-1 inhibitor with potentially be disease-modifying in hematologic malignancies. LSD1 is a member of a group of epigenetic proteins that may regulate gene expression through chemical modifications of RNA and DNA. LSD1 may regulate the maturation of bone marrow cells and is essential for the differentiation of progenitor cells into mature megakaryocytes and granulocytes as well as production of blood cells.

Given that the role that LSD1 may play in the function of blood cell maturation, targeting LSD1 for the treatment of myeloproliferative disorders offers a new potential therapy for these diseases. These diseases are associated with high morbidity and high mortality and remains significant unmet need. Bomedemstat is currently being evaluated in multiple Phase II clinical trials across several myeloproliferative diseases. And the Phase II trial evaluating bomedemstat in patients with central thrombocythemia who have not had adequate control of their platelet counts despite the use of at least 1 standard of care therapy, 95% of patients treated for more than 24 weeks, achieved normal platelet counts with no thromboembolic events. In addition to the improvement in platelet counts, patients also showed improvement in white blood cell counts while maintaining stable hemoglobin levels.

Patients also showed symptomatic improvement with therapy. Of the 12 patients, who had a total symptom score at baseline of greater than 20, 75% showed a total decrease in total symptom scores, and 67% showed an improvement in more than 10 points. Further, 67% of patients demonstrated a net decrease in mutation allele frequencies. This is an important prognostic indicator of myeloproliferative diseases. There were no safety signals identified for bomedemstat. Based upon the Phase II results and our excitement around this novel mechanism, we are planning to initiate Phase III development later this year.

With that, I'll turn the meeting over to Chirfi.

Chirfi Guindo - *Merck & Co., Inc. - Senior VP & CMO for Merck Human Health*

Good evening. Thank you, Marjorie. It's really great to have you at Merck and to have you as colleague. Good evening, everyone. As you've heard from my research colleagues, we're really excited, extremely excited by the data presented today from our oncology pipeline and the potential that we have to really bring these candidate drugs to impact patients around the world. This data also gives you a line of sight into future opportunities that will support Merck's leadership in oncology well into the future.

Today, we're continuing to execute across our broad in-line portfolio, and we're very proud. We're very proud to have reached approximately 1.9 million patients worldwide. And we're improving their lives, we're extending their lives, and we're helping their families along the way. We're working tirelessly to reach even more patients through strong commercial execution and our robust clinical development program.

An important component of our oncology strategy is to improve outcomes for patients by extending into earlier-stage settings. You heard it from my research colleagues over and over this evening. To date, we have made exceptional progress across 8 existing early-stage indications, including adjuvant melanoma, RCC and triple-negative breast cancer. We look forward to potentially launching 10 new indications between this year and 2025 and even more looking into 2026 and beyond.

Our confidence in the opportunity presented by treating patients in the earlier stage settings has increased significantly following the strong launches of KEYNOTE-522 in triple-negative breast cancer; KEYNOTE-716 in melanoma and KEYNOTE- 564 in renal cell carcinoma.

Let me first turn to 522. Eliav said it, we wrote the book, the Merck team wrote the book in I-O. Triple-negative breast cancer, neoadjuvant adjuvant is an important chapter of that book. KEYTRUDA is the first and only anti-PD-1 to demonstrate benefit in neoadjuvant adjuvant, triple-negative breast cancer. As we know, it's an aggressive disease with high rates of recurrence.

This is -- with an established strong screening infrastructure, we have quickly established KEYTRUDA in a leadership position in this setting. And we continue to grow -- to drive growth through KEYNOTE-522.

As the launch matures in the U.S., we see opportunities for continued growth by increasing the proportion of patients who go on to receive adjuvant therapy and through uptake in ex U.S. markets, in particular in Europe, China and Japan, where we have secured approvals.

Moving to KEYNOTE-716. KEYTRUDA is the first and only PD-1, anti-PD-1 adjuvant treatment option approved in patients with Stages IIb, IIc and III melanoma. Since the launch, we have seen strong uptake as well as consensus among panel members of the National Comprehensive Cancer Network, but this intervention is appropriate, as evidenced by recent guideline updates. This has enabled us to quickly establish a leadership position in this setting, and we're continuing to work to reach more patients.

Finally, we're pleased with the launch of KEYNOTE-564, which demonstrated efficacy of KEYTRUDA as an adjuvant treatment in patients with localized RCC at intermediate high or high risk of recurrence following an nephrectomy.

Turning to lung. This is the topic that is creating a lot of excitement in the scientific community here at ASCO. KEYTRUDA is the first and only immunotherapy approved as an adjuvant treatment in these patients. And we're building on this progress by working to expand and reach patients across the eligible segments, particularly in the intermediate high-risk individuals. KEYTRUDA is the first and only immunotherapy approved as an adjuvant in these patients, and we're building on this progress, working to expand across the eligible patient segments, particularly for intermediate high risk. And globally, these indications, these 3 indications, represent a significant portion of our growth. Outside of the U.S., it's still early days, but we're making significant progress, and we are well on our way to create a new standard of care, particularly in triple-negative breast cancer.

Now we can turn to lung. My apologies. I'm getting too excited about it. So as you've seen today, we're building on the wealth of data already established by KEYTRUDA by extending into from metastatic to early stage setting. Non-small cell lung cancer is an important example of this strategy with the recent launch of KEYNOTE-091 and the potential future launch of KEYNOTE-671, which Greg alluded to earlier. Together, we can strengthen our ability to position our company as a leader -- to consolidate our leadership in lung and help so many patients going forward.

If KEYNOTE-091 -- 671 is approved, it would be the only I-O regimen to treat certain patients with resectable non-small cell lung cancer in the neoadjuvant and the adjuvant study, both neoadjuvant and adjuvant settings, regardless of PD-L1 expression levels. We, along with the medical community, are highly focused on improving the current treatment paradigm in the earlier stage lung cancer. And to date, while early, we're extremely encouraged by the uptake that we have seen with KEYNOTE-091.

In contrast with other tumor types like breast, screening rates in the U.S. for lung cancers are very low. Treatment rates are also very low. We have a meaningful opportunity with KEYTRUDA, especially with the compelling data presented here at ASCO to positively impact treatment rates by educating HCPs on the risk of disease recurrence. Let me remind you that historically, the disease recurrence is over 50% post surgery. So we have the opportunity to educate HCPs on the risk of recurrence and the benefit of systemic therapy. Longer term, we have an opportunity to work with provider communities to help improve lung cancer screening and earlier diagnosis through a sustained and growing effort to increase awareness and patient activation. Through these efforts, we're encouraged by the launch of KEYNOTE-091 and the potential of KEYNOTE-671 to position us well into the future and maintain our leadership in non-small cell lung cancer.

To summarize, we have several opportunities that will enable us to sustain leadership in oncology. In the near term, there is a significant opportunity for us to extend into early-stage cancers. We continue to expect that these indications will represent over 50% of Keytruda's annual growth through 2025 and approximately 25% of global KEYTRUDA sales in 2025. In the near term -- in the medium term, we continue to work to broaden the impact of our approved therapies and improve patient access, including subcutaneous formulation, Eliav showed you the rationale on that; core formulations; and combination approaches. As we look into the future, we're advancing our broad pipeline of novel mechanisms, including ADCs and small molecules, which we believe have the potential to achieve sales of $10 billion-plus approaching the mid-2030s. This is on a nonrisk-adjusted basis. Together, these steps give us confidence in our ability to deliver value for patients, for customers and for shareholders over the long term.

With that, I'll turn it back to Dean with my apologies here for technical...

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

Thank you, Chirfi. As you can see from this evening's presentation, we have a broad pipeline that has made an important impact in oncology and will continue to do so. We have multiple agents and a real opportunity to help further improve patient outcomes, and our progress to date continues to inspire us to achieve even more.

Before I open it up for Q&A, I wanted to introduce Scot Ebbinghaus and Gursel Aktan, who are joining us in the front row. Scot has responsibility for our melanoma, gastrointestinal and genitourinary cancers, including renal cell carcinoma and bladder cancer. As highlighted this evening, Scot and his team have played a critical role in the development of our individualized neoantigen therapy in collaboration with Moderna as well as the CYP11A1 inhibitor for metastatic castrate-resistant prostate cancer in collaboration with ORION.

And Gursel heads our women's cancer development program. And the impact we have made in breast and gynecologic cancers is a direct result of Gursel's leadership and also recently described by Chirfi in triple negative breast cancer. So Scot, Gursel and Greg's team continue to push the boundaries as we move from late-stage metastatic disease to earlier stages of cancer. And I look forward to providing further updates on these programs and their progress.

And then with that, let me thank you for your attention, and I'll turn it over to Peter for Q&A.

QUESTIONS AND ANSWERS

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

Okay. Thank you, Dean. We're going to start with questions here in the room. But Holly, if you could provide instructions to those on the line before we get started here.

Operator

(Operator Instructions)

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

Great. Thank you, Holly. So I see a lot of hands already. We're going to try to get to everyone. We're going to have time to go maybe a bit past 7:15 here tonight. But if everyone could limit themselves perhaps to 1 question, that would help us get to everybody. Domini and Steve have microphones here in the room. When they bring in your mic, if you could just state your name and firm, that would be really helpful. Trung?

Trung Chuong Huynh - *Crédit Suisse AG, Research Division - Research Analyst*

Trung Huynh from Credit Suisse. So KEYNOTE-671 in the perioperative setting, caveating cross-sell comparisons, something I know that's a bit naughty, but all of our sell-side analysts do it. But when you look at your trial versus AEGEAN, AstraZeneca's AEGEAN trial, you can have a look at the control arm, and it performs a bit worse. Is there any reasons for that? If I have a look at the study, it's very similar patient population, similar chemo arm. Any reason for that?

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

Greg, eventually Eliav, providing further insight. But Greg, did you want to answer the question?

Gregory Lubiniecki - *Merck & Co., Inc. - VP of Late-Stage Oncology Development*

Yes. Thank you. So when 671 was being designed, the control arm was modeled off of one of the cooperative groups and the outcomes there where neoadjuvant chemotherapy had been used. And that assumption was applied for this analysis plan of KEYNOTE-671, and as it turns out, the control arm performed exactly as had been planned. I think the thing to keep in mind is we're designing clinical trials, is each study is going to need to be evaluated in the context of itself.

There's just the 1 randomization for the patients that were involved in the study and the results are the results. So this was a well-conducted, scientifically valid clinical program yielding some incredible results on the event-free survival, providing that 42% reduction.

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

Nothing more to add?

Gregory Lubiniecki - *Merck & Co., Inc. - VP of Late-Stage Oncology Development*

Nothing more to add.

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

Great. Thank you, Trung. Daina?

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

Daina Graybosch from SVB Securities. I want to ask about V940, your individualized neoantigen vaccine. Two -- maybe a 2-part question. What gives you confidence in the signal despite some misbalances between the arms, notably tumor mutation burden? And do you agree with the hypothesis that the late separation of curves could be due to a slow ramp-up of the T cells? And do you have any technologies that might speed that ramp-up, if you agree.

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

So if you don't mind, can we get -- Scot, do you have a microphone? Why don't you take a first shot at it and Eliav the second shot.

Scot Ebbinghaus - *Merck & Co., Inc. - VP of Late-Stage Oncology Development*

Right. So the second part of your question, I guess, I'll answer first. So we saw the late separation of the curves. I think there are 2 explanations. One is practical. One is likely scientific. The practical one is that it takes some time for them to get the vaccine started. So the vaccine started a little bit later than the pembrolizumab did. Therefore, the -- you would expect those curves to separate a little bit later.

The more scientific reason, I think you're spot on. It takes some time for the vaccine to develop a T cell immune response. Remind me your first question? TMB imbalances, yes. So my recollection is that there may have been some imbalances between the arms, but there was no particular relationship between the outcome and the PD -- and either PD-L1 or TMB expression. So we feel pretty confident. These are pretty -- for Phase II data, I think they're pretty impressive results.

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

Yes. I think that the -- so thank you, Scot, and I agree with you completely. I mean I think that the -- first of all, we did look at adjustments for TMB and other factors. And honestly, I don't think we saw very much to warrant one way or the other. The regimen of administration of the IMT is over a 6-month period. So you're always going to have -- getting a little bit of a delay factor.

And the question about what the implications of that might be for future use, I don't think it's going to be a problem for us because again, these are patients who are in the postoperative setting after having a resection of the visible tumor, all of the tumors removed. And so events -- where the events are really happening, hot and heavy -- and you look at -- you can see that in the curve as well as in the later stage. So I think we're in the right -- we certainly can be able to use that period of time to mount the proper immune responses.

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

Great. Thanks, Daina. Chris Schott.

Christopher Thomas Schott - *JPMorgan Chase & Co, Research Division - Senior Analyst*

Chris Schott, JPMorgan. Just on TROP2, it seems like peers may have a little bit of a time-to-market advantage in this. So can you just elaborate on the confidence you have that you have enough differentiation with your asset to be able to gain share and find a role in the market even if you're maybe a bit later than others who are out there?

And are there opportunities, whether in markets or lines of therapy, that you could actually be first in market is to go about kind of holistically where TROP2 could play a role? Just maybe elaborate a little bit more.

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

So that's great. I think we should hear from Marjorie, who has some experience with antibody drug conjugates. And then maybe Eliav make a comment and then that creates a scientific basis for Chirfi to answer what I would call a more commercial question. Does that sound okay, Marjorie?

Marjorie Green - *Merck & Co., Inc. - SVP Late Stage Oncology Development*

Yes. No, great. Thanks so much for the question. ADCs are not equal. Definitely, we've seen that throughout the history of development of the ADCs. Even if you've got the same target, the way the antibody is developed, how it internalizes the stability and characteristics of the linker and then the payload itself and the ability to get that antibody drug ratio in a certain way. So they're all a little different.

We are confident that we have an active drug. We are also confident that we've got a great foundation with pembrolizumab, that we have a lot of data that we can use to help really be strategic in our development. And Merck has been an execution machine. When you look -- we are behind to nivo, and you can look where we are today. And so I have great confidence in science that we will be very thoughtful about where is their clinical need, where is there a TROP-2 expression and how can we accelerate our clinical studies and execution to where we can benefit the most patients.

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, I really -- thank you, Marjorie. I think that's spot on. One of the things that's important for us is to be able to leverage the platform that pembrolizumab puts forward. And you might say, well, that's very nebulous, but what does that really mean? What it really means for us is that, just like you've seen with 522 and 671, the unique places with pembrolizumab is indicated and others are not. It's not surprising, for example, that the TROP studies are being done with the pembrolizumab backbone, but we're -- we've got pembrolizumab in our toolkit, not there. Trying to do things with intense -- whatever.

But anyway, the point that I'm trying to make is that leveraging pembrolizumab will be very valuable. Doing clinical trials where we've innovated design is very valuable. Having a drug that doesn't have visible evidence currently of ILD is very valuable. The ability then to combine it with other drugs that may have complicated profiles like the other chemotherapy agents are very valuable. So we're going to move forward. As Marjorie pointed out, we have an execution machine.

The gentleman to my right here wrote the book on I-O in lung. That dude over there is the melanoma guy and renal cell. That lady does all of the breast and GYN. And if you look at GYN cancer, there isn't a place that pembrolizumab isn't indicated. So I think that there -- that we're in actually a very exciting position. As I mentioned, as the guy that writes the checks, the ct.gov is going to be pretty busy with Merck products, Merck studies.

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

Chirfi?

Chirfi Guindo - *Merck & Co., Inc. - Senior VP & CMO for Merck Human Health*

Yes, maybe the only thing I'll add, Chris, is just -- let's not forget that 7 to 9 out of 10 patients who receives an I-O today receives KEYTRUDA in all of our key markets. And so we really have an execution machine, commercial engine that is highly, highly productive. And so we are leading in multiple tumor types. We referenced triple-negative breast, more recent launches. And so we believe that the ADCs will really allow us to leverage that platform that Eliav talked about to further reach more patients and enhance our value proposition in a sense.

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

I have to make a comment because I was trying to be really disciplined to get other people to have a chance to talk. But you asked a question about the INT, you asked a question about the TROP-2 and we just finished talking about 091 and 671. I think it's really important to understand that, that issue of going into earlier-stage cancer gives us a platform. It's not just that Chirfi has something to advance the patient. It means that you want to move anything in oncology. You take your best drug in later stage and you move it in earlier stage. That's been the book in oncology at ASCO for the last how many decades.

In order to do that, whether it be INT, whether it be TROP2 ADC, whether it be a KRAS that can finally combine with a PD-1 in metastatic, you're going to want to drive it in earlier stage. So our investment in that earlier stage is not just about product and trying to get more product to patients to do great, but it is a platform that every other compound that looks good can follow in earlier stage. And it's not just a pipeline of products. It's not just the pipeline platform going earlier stage, it's a pipeline of people because if we haven't laid that down, I'm not so sure that Marjorie would be joining.

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

Great. Thank you, Chris. We'll stay on this side of the room, Steve.

Stephen Michael Scala - *TD Cowen, Research Division - MD & Senior Research Analyst*

Steve Scala from Cowen and Company. Eliav, you mentioned no cases of ILD with MK-2870 to date. The presenter at the poster yesterday made that same point. But then he added a couple of other points that were interesting about ongoing trials, presumably also including those in China. For instance, he mentioned that the phenomenon of better efficacy in EGFR-expressing patients has persisted, maybe suggesting that it's not just an anomaly in that there's been no dropouts, and I interpreted that as for any reason, not just ILD.

So can you confirm that all 3 points are true? No ILD, no dropouts in this EGFR outperformance, is true of any patient dosed with this molecule by either company and not just the Merck study?

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

Right. So let me start with the ILD. Obviously, when we talk about ILD, we mean cases of ILD there are significant enterprise therapy and require patients to discontinue their drug. And we'll be able to follow the patients. There's hundreds of patients running clinical trials in China. They're already in Phase III in a couple of indications. So that's good.

Obviously, the EGFR-positive patient population is really valuable. I think we're seeing really great results there, and you'll find that we'll be planning a lot of work in that -- around that particular stratum of patients. That will be really exciting for us. And I think that the tolerability again, has been really quite exceptional. It's true that these drugs, like every chemotherapy, has got a lot of AEs. The difference between, I think, what we see with MK-7264, MK-2870 is that the toxicities are the standard thing, but oncologists have dealt with pretty effectively.

And I think that we are -- we have a pretty decent chance of having a drug that can be used for longer periods of time, and we'll be able to do that in a much larger patient population, not just in China, but of course, in the United States and elsewhere.

I would point out that the SKB trials, while it's true that the majority of them are in China, there is actually -- it is a global study. So there are non-Chinese patients in the SKB study. So just -- I just want to make sure that, that's clear, even though, of course, there's over a percentage of Chinese folks there. But I don't see that as being a big issue from our point of view. We're really excited about the product.

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

All right. Thank you, Steve. We'll go back to this side of the room. Seamus?

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

Seamus Fernandez from Guggenheim Securities. So just -- first question is just on the data with the ctDNA, with the personalized cancer vaccine. Can you just help us better understand why there was such a difference in the magnitude of response without ctDNA, so in the ctDNA negative patients, why there was such a different sort of superior response to the ctDNA-positive patients? It just implies that perhaps a higher tumor burden could be somewhat problematic for treating these patients. I'm just trying to get a better understanding of that.

And then second, if you could, interested to hear how you're thinking about developing 2870, just sort of the pace and the path of development that you see going forward and the importance of TROP-2 as you move forward into the treatment regimens. That's something that I think Merck did uniquely well and really did write the book on in immunotherapy. So just trying to get a better understanding if you think TROP-2 has relevance as you advance forward into treatment, into earlier lines of therapy?

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

So I'll just first start by saying that I just met with my Moderna colleagues, and we almost joke that we were not going to answer any question that started by, hey, can we talk about your cancer vaccine because we need to train all the whole community, call it, individualized neoantigen therapy.

Having said that, given that you asked about INT and the TROP2 ADC, both of them, I'm going to just hand this to Eliav really quickly.

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

Sure. So I think that what you saw with the ctDNA data is a problem that we see in general -- and it's not a problem, it's a phenomenon that we see in general in these early-stage cancer trials. If you're ctDNA-positive, your event rate is pretty high and early. And so I think if you look at -- and you've now -- this is a slice and dice to very small numbers. The INT has benefited in both positives and negatives. It's just a matter of how quickly the endpoints accrue. And you can imagine in the ctDNA-positive patients, there's -- the endpoints accrue pretty quickly because those patients actually still have active tumor. Even though you might not have seen that, it's going to pop soon enough. And so I'm actually not too worried about this.

I think that we're going to ramble through. And I think you're just going to see that the benefits are going to be pretty good, but probably take a little longer to occur as we have more and more patients in this program.

And then you asked about TROP2. And you're right. I mean I think that the question about biomarkers is going to be really essential. PD-L1 was really a critical way in which we were able to help doctors navigate through the different kinds of patient populations, therapies, et cetera. And that approach is something that we're really keen on taking on here. And it comes from the fact that we -- that with the Kelun interaction and the fact that they're just -- they have multiple, multiple candidates that are coming into the clinic, the idea that we would develop all of them in unselected populations is pretty insane. It doesn't make sense because there's a lot of overlapping coverage.

Now obviously, the early studies have to do that so that we can develop the principles around cutoffs and whatnot. But I'm with you that Merck is really quite good at figuring out where the cut point is and where the way that you can maximize return for patients, not return for us, but return for patients, which is the most important thing and make sure that they get a good bang for the buck. I would tell you that our clinical program is going to be pretty big. And we'll start off with gathering that kind of information, which eventually led us to the place where we got to -- the 22C3 and the less than 1, 1 to 50 and 50 greater than 50, that's now characterized in the field.

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

I just want to add, because the question that you posed about TROP2 and ADCs. It depends on how you look at what the world might look like. Do you think there's going to be 2 to 3 unselected ADCs in the world? Or do you think there's going to be a world where there is going to be potentially multiple ADCs that is not unselected, that all of them are somewhat selected?

And if you view it that way, then I would ask you, what do you think the trajectory of the speed of the field will be? And also, how important is it to show combination benefit with pembro? And how important is it that a company that has executed both clinically and commercially biomarkers, how much of an advantage might that be if that world should come up? So I love your question, but it also partially answer your question as well.

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

Thank you, Seamus. Jon Miller.

Jonathan Miller - *Evercore ISI Institutional Equities, Research Division - VP*

Jon Miller from Evercore ISI. I want to -- maybe I'll start with the commercial question. Chirfi hasn't gotten a lot of airtime here. On the early-stage indications in general, I don't just mean lung, but early stage in general, what's current penetration of I-O in -- for instance, in lung, either adjuvant or neoadjuvant setting currently because obviously, there are other things approved there in various combinations?

But you said that a big part of the commercial opportunity was expanding, health care provider understanding use of these drugs in the adjuvant setting. So what's the untapped potential of that market beyond what currently approved options are already penetrating?

Chirfi Guindo - *Merck & Co., Inc. - Senior VP & CMO for Merck Human Health*

So maybe the most recent example we have is triple-negative breast cancer, where we launched 522. We're still in the launch phase, in many cases. We launched it in the U.S., as you know, with a very, very nice uptake. We're seeing very favorable uptake in the U.K., in France, in Germany and Japan, where we have secured reimbursement. And then we will be seeing uptake in other countries going forward.

The advantage that we've had in this case is that there was a well-established concept in triple-negative breast cancer. So we could execute the education programs, linking surgeons with medical oncologists, educating the community. You can do that fairly quickly and which led to really uptakes, majority of cases really receiving KEYTRUDA in the next -- in the first 6 to 9 months of launch in all of the countries that I just mentioned. It's been very, very rapid. We do not anticipate that kind of speed of uptake in the case of lung because it's going to be a heavy lift.

There's no established concept of treatment in the same way of screening to diagnosis, to treatment post surgery in the same way that we have experienced that in triple-negative breast cancer. But we are committed to really taking the learnings from KEYNOTE-522 and applying those to KEYNOTE- 671 once, hopefully, we get that through the finish line. And in the meantime, KEYNOTE-091, which is also in the launch phase in the adjuvant setting, is showing a lot of promise, as I said in my presentation.

So this is a long-winded answer to say it's still early days. We are very, very excited by what we hear from the scientific community, the uptakes we've witnessed so far, but we still have a long way to go, but there's a huge opportunity going forward. Let's not forget that in lung, more than 50% of patients will have recurrence post surgery. So there's a huge unmet need, and we are going to partner with the community, with the societies to really educate physicians, surgeons, in particular, and connect them to medical oncologists so patients can get treatment.

Jonathan Miller - *Evercore ISI Institutional Equities, Research Division - VP*

Maybe just a quick follow-up on the Moderna collaboration, Dean, I won't call it a vaccine. But one of the things that discussed and mentioned was the lack of correlation between RFS and DMFS in that study. Marking is quite distinct from other adjuvant studies in the indication, which seem to fall really directly on the line. Is that mechanistic? Is that something to do with the trial? Was there anything to read into that?

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

Scot, do you want to take this one?

Scot Ebbinghaus - *Merck & Co., Inc. - VP of Late-Stage Oncology Development*

Yes. So I think what the discussion was pointing out was that DMFS actually looked better than RFS, which is a little surprising. We, actually, at the very same session right before that, presented the final DMFS analysis of KEYNOTE-716, which is what established pembro as a monotherapy in Stage II melanoma. And the DMFS and the RFS were pretty much aligned directly with each other.

Whereas in the case of the Phase II study with the INT compared to -- plus pembro, compared to pembro, DMFS actually outperformed RFS, which is a little surprising. I don't know how much to read into that, given it's a Phase II study. I think it's encouraging. Ultimately, the goal of an adjuvant therapy is to prevent patients from having distant metastases and prevent them from dying because that's what patients die from. But it's an interesting observation.

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

Mohit?

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

I have a question in half. Sorry, Peter. So one question. TROP2, if you look at the AZ's TROP2 versus your TROP2, the safety profiles are a little bit different. One has ILD, one has those neutropenias and lymphopenia. So from the combined ability point of view with pembro, which one is easier to handle? And half question, I promise, I thought of it by myself, which one was the most surprising data at ASCO?

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

Do you want to take this, Greg, and Marjorie, take the TROP2?

Marjorie Green - *Merck & Co., Inc. - SVP Late Stage Oncology Development*

Yes. No, thanks so much for the question. Just I think cytopenias make it a little bit easier to combine. The physicians know how to handle them. When you look at the cytopenias that were reported, they didn't result in any treatment discontinuation. The other thing is to recognize that in many studies conducted in China, the reporting of laboratory values report as an AE, whether or not there's clinical significance.

And so I think as we see these drugs continue to develop, as we start to combine more, we'll get a better sense. But I think that because KEYTRUDA can cause pneumonitis, that being able to handle cytopenias would be easier, but I'd love Greg's thoughts on that as well.

Gregory Lubiniecki - *Merck & Co., Inc. - VP of Late-Stage Oncology Development*

No, I agree that one of the nice things about pembrolizumab has been the ease with which it combines with most other agents. There are a few where it does not. And so we certainly know that it can combine well with more generalized cytotoxic chemotherapy. And so we anticipate its ability to combine with TROP2 to be quite manageable.

As Marjorie was saying, physicians are used to dealing with cytopenias. And just because of the extensive number of indications that pembrolizumab is in now, they're also used to managing AEs that can come from immunotherapy, such as pneumonitis as well.

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

So I'm going to take the most surprising thing. And the most surprising thing is you see the movement of fields, and I kept talking about early-stage cancers. You've seen -- and I need to be very careful. I'm answering this because of 671 and 091, but not just because of 671 and 091. Let's just take lung cancer. You see a movement. When you see the OS that's not statistically significant, this is an IA1, right. You sit there, earlier stage cancer, you start looking like a cardiovascular outcome trial in my field, and you have that jaws look like that at IA-1. That's pretty stark. And the reason why I think that's important is that when you see not just us, but other companies moving into earlier stage, you have a real opportunity to use early screening to treat for the possibility of cure. It's not just us. It's the whole field is moving that way. And I think it's very important for all of us to understand that movement.

We also have to understand that if you look at KEYNOTE-091, I think that opened in 2015. It took 8 years. KEYNOTE-671, I mean, IA-1, we're kind of lucky that it's unbelievably striking. That opened in 2018. You're talking about 5 to 8 years to do these trials in earlier stage. And what surprises me here is that many people are walking around and having no understanding that with this great opportunity where they talk about cancer moonshot to get on that shuttle to cure in this, it's real. It's real. But there is an O ring that has been laid out by the IRA. When you look at it, everyone knows in cancer, you start in late stage, you prove it, you get approved. And then you go into earlier stage because you know what the relative benefit risk is.

In the situation with the IRA, I get an approval here. What is the investment you're going to make for 5- to 8-year study in earlier stage given the IRA. It's one thing to say 9 years for a small molecule, it's 13 years for biologic. But you have very significant people in some of the caucuses, who are actually talking about 5 and 5. So what is really surprising to me is a lack of energy around the fact that right at the moment that you can grasp victory, it's in your hands, you're going to grab defeat.

It's as almost as if that shuttle that we could land in earlier-stage cancer, we've just put a faulty O-ring in the Inflation Reduction Act, which is really an Innovation Reduction Act. That is the most striking thing.

And if any specialty should get it, I'm a cardiologist, it will affect cardiology. It will affect other therapeutic areas.

But every one of you have followed oncology and every one of these oncologists have followed oncology, you know this is what's the impact. The impact in oncology will be greater than in the therapeutic areas. The fact that, that wasn't ever discussed or even realized by this audience here is the most striking.

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

So we're going to keep going. I know we have a lot of hands up, and I think we have a few questions on the line. But Terence?

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

Terence Flynn, Morgan Stanley. There's some competitive TIGIT data out at ASCO, both lung cancer, liver cancer. Just wondering if you could offer your perspective on TIGIT as a target broadly and when we might see some data from your program.

And the other is there's a couple of competitors moving in LAG-3 for lung cancer. Just wondering if you might have similar thoughts at advancing on that front?

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

I'm going to give it to you and then I'm going to just make a real quick comment.

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

Sure.

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

So I think we're continuing to be interested in TIGIT and continue to be excited in TIGIT. The issues that we see with the current clinical studies is that their Phase II trials, but also that the comparator is the wrong one. It should be pembro because that's where the action is. And so what we -- where we've, I think, distinguished ourselves is that we did do that. That is where the -- that was a competitor when we looked at our own TIGIT molecule and made choices around the potential opportunities for TIGIT and where we placed our bets.

So I look at it as interesting. I look at it as potentially good, but also mindful that Cityscape was that, and we're still waiting to hear what happens with other studies and the same may very well be true with the ARCUS molecules. We'll be -- I'd like to use the analogy of the cakes in the oven, and it's baking, and hopefully, we'll be able to have some really nice results soon enough. But we're still very strong proponents of that because we were able to do our own studies against the standard of care, which is pembro, and saw some good early signals. But you do Phase III to be able to make sure that what you saw in Phase II was real. So we'll wait and see.

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

So there's not just cake baking, but we put some more cake in the oven, right, for TIGIT, which is to go into earlier stage answers. So I just -- I think I've talked to many of you in the past about how I-O, I-O in late stage is an important place, but I-O and I-O in earlier stage may be a really important place. That's a place where the number of cells that you have to kill is much less, where you can debulk because of surgery, and the immune system is better. So the way that I would answer our view of pembro TIGIT is if we didn't have confidence in it, we wouldn't have started a trial.

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

When did you start? Last year?

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

December of last year. And you said about LAG-3, again, I think these mechanisms are interesting. We have a LAG-3 molecule as well. We have a variety of other medicines that are also, other immunostimulants that are cooking as well in field in our pipeline. You can see that. We'll see.

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

Carter, and then we'll go to the phone.

Carter Lewis Gould - *Barclays Bank PLC, Research Division - Senior Analyst*

Great. Carter Gould from Barclays. Prior to the individualized neoantigen therapy that emerged last fall, there was SWOG data on neoadjuvant adjuvant KEYTRUDA in monotherapy. And one of the surprising things here at this meeting is the extent to which that's been adopted by the academic community, though there was some presentations on it. Does that complicate your positioning? Or is it planned to be integrated into your Phase III plans, particularly just given the protection that offers for those patients that would otherwise relapse in the first 12 weeks of therapy that would otherwise be excluded from your INT?

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

Yes. So you were talking about that SWOG data this past fall. Did you want to -- Scot, why don't you take that? And then I think the question was related to INT in relationship to that.

Scot Ebbinghaus - *Merck & Co., Inc. - VP of Late-Stage Oncology Development*

Yes. So the SWOG 1801 data, I think, is what you're referring to, and that's the trial where they basically tested pembro versus pembro and did the 3 treatments before surgery and 14 after versus just all of it afterwards. And it showed a very nice RFS improvement for starting with the treatment preoperatively and has led to a lot of sort of scientific hypotheses, having some of the tumor sort of in situ may help with the immune response.

I think we can use that when appropriate and exploit that in INT therapy. And that's something that we're certainly discussing at great length. I think there are a number of places where sort of the neoadjuvant-adjuvant paradigm is already in place, and that makes it a really natural fit. So if you can imagine a tumor type, recently 671, where adjuvant, neoadjuvant with pembro already is showing a high degree of activity, adding on the INT in the neoadjuvant space would be a very interesting approach.

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

Yes. And I think that the -- if you -- I'm not concerned about the different paradigm shift there because I think that particular instance is, of course, in Stage III bulky disease tumor that you can see and feel. So I think that, that's going to be interesting for that particular segment, but that's a relatively small segment. If you think about as we roll out the V9401 study, what you'll see is that we're taking more of the 716 plus KEYNOTE-054 approach, which is looking at the entire spectrum of the place where pembrolizumab is indicated.

So while that the neoadjuvant-adjuvant data are really exciting, and I think people are interested in it, I don't think it's going to be particularly impactful to the conduct of our program.

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

Great. Holly, can we take a few questions from the line, please?

Operator

The first question is from Louise Chen.

Louise Alesandra Chen - *Cantor Fitzgerald & Co., Research Division - Senior Research Analyst & MD*

So I just wanted to ask you, do you think the SKYSCRAPER readout coming in third quarter this year would potentially change the human paradigm for non-small cell lung cancer, even if it shows a positive OS benefit? Or would that not really matter at this point?

And then secondly, I wanted to ask you, which of your oncology assets that read out this year at ASCO generated the most buzz in your view?

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

Why don't I give you, the SKYSCRAPER, Greg. I didn't quite hear the whole thing because it broke up. And then I'll give you the buzz question.

Gregory Lubiniecki - *Merck & Co., Inc. - VP of Late-Stage Oncology Development*

Thank you. So in -- if SKYSCRAPER were to show some positive data later this year, I mean, certainly, we'd have to look at what the extent of the data are, there can be statistically significant studies that may not be very clinically impactful. And we'd have to see what that is. But the studies that we have ongoing currently, I don't think that, that readout would change any of the trials that we're doing now since it's important to what the standard of care is when the studies are established, and I think they will still have relevance when the Merck studies read out.

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

And I think that the -- I would point out that the -- it goes back to what the control arm is. And the control arm, in many of these cases, is atezo, and I'll leave it at that.

In terms of the -- what's the buzziest for us, it really depends on the treating physician. 671 was -- we've had like dozens and dozens of meetings, and 671 was all the rage really. I think people are really, really excited about it. And a lot of people are interested in 2870 as well because I think that the idea here is a combination of pembro and 2870 and the ability to apply that across the board and across the spectrum of early and late disease. So I think that, for us, that's been a pretty big deal.

I suspect that Moderna has gotten most of the questions and interest around the INT. So maybe that's -- there's a little bias in that regard. But I think that both 671 and 2870 got a whole lot of exciting questions. And when I met with scientific leaders throughout the 3 days, it's just been nonstop one or the other.

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

The next question, Holly.

Operator

The next question is from Colin Bristow with UBS.

Colin Nigel Bristow - *UBS Investment Bank, Research Division - Analyst*

Thanks for all the detail in this event. It's super helpful. Maybe just a follow-up on TIGIT. I was just curious to get your thoughts on the concept of using FCs versus a competent approach. And obviously, what made you choose the competent approach with in vivo versus even potentially an enhanced approach?

And then maybe just a quick sort of housekeeping one with ctDNA 942. Should we expect to see this used as a stratification factor in Phase III given the imbalances, et cetera, and what we saw in IL-2?

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

I forgot to write this down. So the first one is...

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

It was about TIGIT and FC silent versus competence.

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

Right. And so in the second one, Scot?

Scot Ebbinghaus - *Merck & Co., Inc. - VP of Late-Stage Oncology Development*

So the question was given what was seen in KEYNOTE-942 with ctDNA, are we planning to use ctDNA as a stratification variable in the Phase III? At the moment, we are not planning to use it as a stratification variable, but we are planning to collect specimens to be able to analyze. And I'll just add that in the context of metastatic -- or not metastatic, excuse me. In the context of adjuvant melanoma, we have other, much larger studies and data sets that can help to inform the utility of ctDNA as a stratification variable or as a patient selection variable. And we'll be looking at those other studies that we've done in -- with pembrolizumab and metastatic melanoma to help inform that very question.

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

So I was just going to quickly answer the TIGIT, which was about FC-competent and non-comp. I mean what I would just basically say is I actually was an oncology discovery. And I can tell you the preclinical evidence that we have as to why we chose what we chose is very clear. However, getting to the question is it's all fun and games until you play it out in the human. So we'll have to just see what the clinical data is. But our choice was driven by compelling preclinical evidence.

But I don't want to play that up too much. I'm sure that the others who chose a different path might say that there's preclinical evidence suggested what it is. But it was clear preclinical evidence that led us to make the choices that we made.

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

Final question, Holly, from the line, please.

Operator

Our last question is from Tim Anderson with Wolfe Research.

Adam Jolly - *Wolfe Research, LLC - Research Analyst*

This is Adam on behalf of Tim Anderson at Wolfe Research. On your neoantigen therapy with Moderna, can you comment on the data that you have in non-melanoma tumor types? We're trying to understand if the decision to advance into non-melanoma tumors is because you have some compelling early findings in those cancers? Or if it's primarily based on the results you've seen in melanoma? And also, just to be clear, these next studies you'll be doing in non-melanoma cancers, these are not Phase III studies, correct?

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

Eliav, do you want to take that?

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

Sure. So we also have a Phase I study called KEYNOTE-604 that was -- 603, sorry, 603 that was -- sorry, I got my number wrong -- 603 that had the -- that had some important Phase I results, which are in lung. And I think that those are very important results as well and gave us a lot of confidence. So my answer, in terms of the second question, no, that is not true. We are going to -- the non-melanoma studies will be a mix of Phase II and Phase III studies favoring Phase III.

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

Yes. I just want to add one point, which is we have a clear strategy. We have a probe, a physiologic probe of immune sensitivity, and it's called KEYTRUDA. And we have that advantage, and we're going to use that advantage. So when you throw out melanoma, non-small cell lung cancer, that is playing to our strength, both scientifically and where we are positioned clinically and from an execution.

There are other companies, who have neoantigen therapies. They do not have the advantage that we have. And they have made other choices than we have partially because they may believe it scientifically and also partially because they may not be positioned like we are. Having said that, we are very open that we look at their data to ask ourselves, should we be trying a different strategy.

So we're confident in our strategy, but we're not blind to the fact that other people are, for example, putting it in tumors that there's very little evidence of immune sensitivity by previous PD-1s. But should they get compelling clinical responses, not preclinical or test tube sort of responses, true clinical outcomes data, of course, we will look at that data, and we will change and adapt and adopt accordingly. But we're going to play to where we have an advantage and where that advantage makes scientific sense.

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

Okay. Thank you all again for making the trip out here and being with us. We appreciate the interest and the great questions. And unless Dean has any closing comments, we'll say goodbye, but thank you very much. Dean?

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

I think that I want to thank all of you for joining us. I think I'll see some of you next week.

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

Next week, Goldman Sachs.

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

And so thank you very much for taking the time in a very long arduous weekend for all of you. Thank you very much for joining us, and we will see you soon.