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## PRESENTATION

**Operator**

Good afternoon. My name is Lara, and I will be your conference operator today. At this time, I would like to welcome everyone to the Merck & Co. Oncology Event at ASCO 2021 Webcast Conference Call. (Operator Instructions) I would now like to turn the call over to Peter Dannenbaum, Vice President, Investor Relations. Sir, the floor is yours.

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

Thank you, Lara, and good evening, everyone. Welcome to Merck's 2021 ASCO Investor Call. Dr. Dean Li, President of Merck Research Labs, will lead off our presentation with an overview of our oncology program. He will be followed by Dr. Roy Baynes, Head of Global Clinical Development, who will provide Merck's ASCO data highlights; Dr. Vicki Goodman, Head of Late-stage Oncology Development; and Dr. Eric Rubin, Head of Early-stage Oncology Development, will provide insights into several of our development programs; Jannie Oosthuizen, Head of Oncology Human Health, will provide a commercial perspective; Frank Clyburn, President of Human Health, will be available for the Q&A portion of our call, which will follow the presentations.

Before we get started, we would 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 United States 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.

Our SEC filings, including Item 1A in the 2020 10-K, identify certain risk factors and cautionary statements that could cause the company's actual results to differ materially from those projected in any of our forward-looking statements made this evening. Merck undertakes no obligation to publicly update any forward-looking statements. The slide deck being used for today's call has been posted to our website.

With that, I turn the call over to Dean.

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**Dean Y. Li** - *Merck & Co., Inc. - EVP*

Thank you, Peter. I'm excited to be here today with my colleagues from MRL and Human Health to talk to you about how we are progressing our strategy in oncology, including data at ASCO highlighting results in early-stage disease and novel mechanisms.

At Merck, we are in a unique position to make a difference in the oncology treatment landscape and continually improve outcomes for people with cancer. We have a broad oncology portfolio of innovative early- and late-stage assets and the expertise and ability to leverage KEYTRUDA where appropriate. And something that Jannie will touch on later is the significant commercial potential here. Because of the data and our commercial capabilities, we are well positioned to execute commercially and compete in this market.

Now we've made tremendous progress in the treatment of cancer with KEYTRUDA with demonstrated activity in over 30 cancer types. We are making a real difference in patients' lives. KEYTRUDA now has 29 approved indications in 16 cancer types, including 2 tumor-agnostic indications, an increase of 5 new indications over the past year, including in important tumor types such as triple-negative breast cancer and MSI high colorectal cancer.

We have been able to demonstrate improved cancer outcomes across more than 25 of our monotherapy and combination study thanks to exceptional clinical execution. These 2 slides represent what has been done to date. We are not done. We are confident that we will continue to demonstrate survival benefits across additional cancer types and in earlier lines of therapy, with nearly 80 Phase III studies ongoing to evaluate a survival benefit across more than 20 cancer types. Our continued momentum, highlighted by the data at ASCO, further reinforces the successful implementation of our strategy in oncology. We are continuing to establish KEYTRUDA as a foundational treatment and expanding to additional tumor types and to earlier stages of disease.

In addition, we are targeting new areas of research like hematologic malignancies by the addition of new candidates within our oncology arsenal. We are deepening the response of our medicines and extending the benefit for patients into various cancer types through use of combinations. We are also extending the value of our medicines to more of patients with our Q6 Week dosing regimen. And in addition, we have studies evaluating subcutaneous administration. Innovation around dosing and routes of administration can profoundly impact the lives of patients and their families.

Our pipeline is advancing in part due to strategic collaborations and acquisitions that have given us access to innovative assets that have resulted in a broader portfolio, with more opportunities to improve patient outcomes. And finally, we remain steadfast in our commitment to biomarker research and to identify patients who are most likely to respond to treatment. We are building on our leadership with a significant progress in the treatment of cancer.

Now all of this has set us up to have one of the industry's broadest and most diverse immuno-oncology programs. These efforts alone have the potential to meaningfully increase the number of patients whose lives can be impacted by our oncology portfolio. We are very well-positioned and have the necessary momentum to become the market leader in oncology, which Jannie will speak to in a few minutes.

Where we have the opportunity to triple the number of new indications and launches over the next 8 years, we are poised to deliver more than 90 potential new indications by 2028, including a substantial portion from new molecular entities, with over 50 of those expected by 2025. We have made tremendous progress in oncology, fueled by the momentum we've established with KEYTRUDA as a foundational cancer treatment. We have been actively diversifying our portfolio through corporate partnerships, through acquisitions, through internal discovery and through external collaborations that span discovery through clinical development.

We are increasing the impact we have on patients' lives. Vicki and Eric will describe several of our early- and late-stage assets that we believe helps set us for sustaining and enduring success in oncology throughout this decade and well into the next.

I will now turn the call over to Roy for an overview of key data in earlier lines presented at ASCO.

**Roy D. Baynes** - *Merck & Co., Inc. - Chief Medical Officer*

Thank you, Dean. With more than 200 abstracts submitted, we will focus on just a small subset of our key data. The first area for focus will be new data in the setting of treatment of early-stage disease. Next, I will highlight each, emphasizing highly meaningful clinical benefit in recently completed studies and durable outcomes in completed studies. And finally, I will cover data relating to some novel therapeutic agents.

We have the great privilege to have 2 of 5 plenary presentations at this year's ASCO, where one showcased the first presentation of the positive KEYNOTE-564 study of pembrolizumab in the adjuvant treatment of surgically resected renal cell cancer. The second was first presentation of the positive OlympiA study of adjuvant Lynparza therapy in high-risk primary breast cancer that was mutant for the BRCA gene and was HER2 negative. In addition, there was the first presentation of the final RFS analysis of the SWOG-conducted KEYNOTE-053 study of pembrolizumab compared to either interferon-alpha or ipilimumab in the adjuvant treatment of Stage III melanoma. Immature OS data were also shown at this final analysis.

These 3 early-stage readouts should be seen in the context of our recent top line release of KEYNOTE-522, reaching its dual primary end points of pathologic complete response and event-free survival in the perioperative treatment of primary triple-negative breast cancer. We were also able to present, for the first time, the data from KEYNOTE-811, which supported accelerated approval of pembrolizumab plus chemotherapy plus trastuzumab in the frontline treatment of advanced HER2-positive breast -- gastric cancer.

Data was shown relating to encouraging quality-of-life observations in KEYNOTE-581 and KEYNOTE-775, which had recently been shown to have highly significant and clinically meaningful improvements in all major end points for the combination of pembrolizumab and lenvatinib in frontline treatment of renal cell cancer regardless of risk category and second-line treatment of endometrial cancer, respectively.

We were able to show the durability of clinical benefit of pembrolizumab monotherapy in cis-ineligible and all platinum-ineligible frontline treatment of metastatic urothelial cancer and in the second-line treatment of metastatic urothelial cancer. We provided the final analysis of KEYNOTE-426, which was indeed the first study to establish the role of pembrolizumab plus a tyrosine kinase inhibitor in the form of axitinib in the frontline treatment of advanced renal cell cancer regardless of risk category.

Finally, I will summarize our first presentation of a novel agent in the form of favezelimab, our LAG-3 antibody in combination with pembrolizumab in microsatellite-stable colorectal cancer. Note also, we had a presentation of our HIF-2 alpha-antagonist, belzutifan, in renal cell and nonrenal cell tumors in patients with von Hippel-Lindau disease. Here, we reported progressive increases in response rates as a function of longer exposure. These data are really important as in sporadic renal cell cancer, a hallmark of this cancer, is loss of VHL function, either by mutation or methylation.

In KEYNOTE-564, adjuvant pembrolizumab reduced the risk of disease recurrence or death by 32% at the first interim analysis in patients with renal cell cancer after surgical removal. While immature for an overall survival analysis, there was a very encouraging favorable survival trend, with a 46% reduction in death at this early time.

It should be noted that higher-risk renal cell cancer treated with surgery has about a 50% rate of recurrence. This is the first positive adjuvant study for an I-O agent in this setting and indeed one of the first demonstrations of positive benefit risk of any adjuvant treatment in this setting. These results are statistically significant and clinically very meaningful and if approved, will be practice-changing.

In the OlympiA trial, the adjuvant use of olaparib adjuvant therapy in patients who had undergone surgery and perioperative therapy for BRCA-mutated HER2-negative high-risk primary breast cancer resulted in a 42% reduction in the risk of invasive disease recurrence, a 43% reduction in the risk of distant disease recurrence and at this early time point, a directionally very encouraging trend of a 32% reduction in the risk of death. These results are statistically significant and clinically very meaningful and if approved, will be practice-changing. The implication of these data are that BRCA testing should become standard in informing patients of their therapeutic options.

Next, I will briefly discuss our data presented for the first time for favezelimab, our LAG-3 targeted antibody, which in advanced third-line-plus microsatellite-stable colorectal cancer, in combination with pembrolizumab, showed a very respectable response rate, disease control rate and duration of response. As a reminder, approved agents in this setting typically show low single-digit responses, and this is truly an area of great unmet medical need. We are advancing this combination into a Phase III study.

At the recent GU meeting, we have the privilege to present the first readout of KEYNOTE-581, a study of the combination of pembrolizumab and lenvatinib, and demonstrated a significant improvement in progression-free survival with a hazard ratio of 0.39 and overall survival with a hazard ratio of 0.66 versus sunitinib in the frontline treatment of metastatic renal cell cancer regardless of risk category. In the data presented here at ASCO, health-related quality of life was directionally improved in these patients with the combination. These data are currently under priority review with the FDA.

In a similar vein, at the recent Surgery Gynecology Oncology meeting, data for this combination was shown for the first time demonstrating significant improvements in progression-free survival with a hazard ratio of 0.56 and overall survival with a hazard ratio of 0.62 versus physician's choice of chemotherapy treatment in the second-line therapy of advanced endometrial cancer, both in patients with proficient mismatch DNA repair status and in all-comers. In the data presented here at ASCO, health-related quality of life was presented, confirming an overall positive benefit risk ratio in these patients with the combination. These data are currently under priority review with the FDA.

In KEYNOTE-811, the combination of pembrolizumab, chemotherapy and trastuzumab was associated with a highly significant and clinically meaningful 23% increase in response rate compared to chemotherapy plus trastuzumab alone. This recapitulated what we have seen in Phase II. The depth of response and the duration of response were also improved. This was the basis for the recent accelerated approval in frontline treatment of advanced HER2-positive gastric cancer. This recent approval is seen as practice-changing.

Finally, I would like to highlight some very important long-term data in the setting of genitourinary malignancies. First, we were able to update the long-term benefit of pembrolizumab in KEYNOTE-052 which studied cisplatin-ineligible patients with untreated advanced metastatic urothelial cancer. After 5 years of follow-up, the overall response rate was at 29%, and this was observed across the entire population. The initial results had initially shown a response rate of about 24%. 40% of the patients with these responses retained their response at a 4-year landmark analysis. It's important to note that before the advent of I-O monotherapy, most such patients did not receive therapy and had a very short overall survival.

Next, I will mention the 5-year follow-up of patients with second-line treatment of metastatic urothelial cancer, where over these 5 years, benefit in terms of ORR, PFS and overall survival were confirmed for patients receiving pembrolizumab monotherapy. In a final analysis of KEYNOTE-426 with some 42 months of follow-up, the combination of KEYTRUDA and axitinib continued to demonstrate clinically significant improved efficacy compared with sunitinib for previously untreated renal cell carcinoma patients regardless of risk category, with an overall survival hazard ratio now of 0.73 and a complete response rate of 10% versus 3.5% for sunitinib. As a reminder, this was the first I-O tyrosine kinase inhibitor study to show an equivocal survival benefit in renal cell cancer regardless of risk category.

I would now like to introduce Dr. Vicki Goodman to you. Vicki is our TA Head for Oncology, Late Development. We are most pleased that she joined us just about a year ago. She is an extraordinarily accomplished oncology drug developer, having previously worked at FDA and having led oncology teams at both GSK and oncology development at Bristol Myers Squibb. She hit the ground running here at Merck about a year ago and is actively engaged in advancing our oncology efforts on a wide array of fronts. Vicki?

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**Vicki Goodman**

Thank you, Roy. It's a pleasure to be here with you all today. I'll focus my presentation today on 5 pipeline assets currently in late-stage development in both solid tumors and hematologic malignancies: 2 small molecules, MK-6482 or belzutifan and MK-1026; and 3 monoclonal antibody checkpoint inhibitors, MK-7684 or vibostolimab; MK-1308 or quavonlimab; and MK-4280 or favezelimab. I'll start with belzutifan.

Belzutifan is first-in-class inhibitor of the transcription factor HIF-2 alpha, which has demonstrated promising activity in both von Hippel-Lindau disease-associated and sporadic clear cell renal cell carcinoma or RCC. In both conditions, loss of function of the VHL protein mimics hypoxic conditions by preventing the degradation of the alpha subunit of HIF-2, allowing it to enter the nucleus, bind HIF-1 beta and activate transcription of hypoxia-responsive genes, which promote angiogenesis and cell survival.

Inhibition of HIF-2 alpha by belzutifan prevents the heterodimerization with HIF-1 beta and inhibits transcription of hypoxia-induced genes, including VEGF. Von Hippel-Lindau or VHL disease is a rare autosomal-dominant genetic disorder leading to loss of the VHL protein and characterized

by multiple organ growth of both benign and malignant neoplasms frequently including renal cell carcinoma. There are no approved systemic therapies specific for VHL.

Belzutifan was evaluated in a Phase II study of patients with VHL and clear cell renal cell carcinoma, and updated data from this study presented at ASCO demonstrated a response rate of 49%, increased from 36% as previously reported, with over 90% of patients exhibiting some degree of tumor shrinkage. Activity was also seen in non-RCC neoplasms in this group of patients, including pancreatic lesions and retinal and CNS hemangioblastomas.

Based on the data from this study, belzutifan has received breakthrough designation from FDA, and a first-ever issued innovation passport from the U.K. MHRA. An NDA has been submitted and is currently under review by FDA with a September 15 PDUFA date.

Loss of VHL is also present in up to 90% of sporadic cases of clear cell RCC, the most common type of RCC. And belzutifan has also demonstrated activity in patients with previously treated sporadic clear cell RCC. On the basis of these data, 3 pivotal Phase III studies of belzutifan, either as monotherapy or in combination with VEGF inhibitors and/or pembrolizumab, have been initiated across multiple lines of therapy in advanced RCC.

I would now like to discuss 3 of our checkpoint inhibitor programs, all of which are being developed as co-formulations in combination with pembrolizumab. Vibostolimab is a checkpoint inhibitor targeting T cell immuno-receptor with Ig and ITIM domains, also known as TIGIT. TIGIT is expressed on effector T cells as well as NK cells and binds to the ligand CD155 or PVR, with higher affinity relative to the co-stimulatory molecule CD226. Potential mechanisms of TIGIT inhibition of tumor immune recognition and killing include inhibition of NK cell-mediated and CD positive T cell-mediated tumor killing as well as induction of tumor suppressive dendritic cells and alteration of CD8-positive cell differentiation and priming.

The lead indication under development is non-small cell lung cancer, where data presented at ESMO last year from a cohort expansion of the combination of vibostolimab and pembrolizumab demonstrated promising activity across all levels of PD-L1 relative to historical controls treated with pembrolizumab monotherapy. We have recently initiated 2 late-stage studies in non-small cell lung cancer, a randomized Phase III study of the co-formulated MK-7684A compared to pembrolizumab monotherapy in patients with PD-L1 expression of 1% or greater and a 3-Arm Phase II study in patients previously treated with checkpoint inhibitors and platinum chemotherapy.

This study will evaluate MK-7684A in combination with docetaxel, or pembrolizumab, in combination with docetaxel versus docetaxel monotherapy. Vibostolimab, in combination with pembrolizumab, is also under evaluation in signal-finding cohorts in additional tumor types, including melanoma and metastatic castrate-resistant prostate cancer.

Quavonlimab is an inhibitor of the checkpoint CTLA-4 expressed on T cells. CTLA-4 mediates immunosuppression by binding to B7 on antigen-presenting cells with higher affinity relative to the co-stimulatory CD28, thus reducing T cell activation in the presence of tumor antigens. Quavonlimab, co-formulated with pembrolizumab, MK-1308A, is currently being evaluated in 5 tumor types, including hepatocellular carcinoma, where it is being studied in combination with lenvatinib; in melanoma; and in MSI high colorectal cancer, where a Phase II study was recently initiated. A Phase III registrational study in first-line advanced renal cell carcinoma began enrolling in April and will test the combination of MK-1308A in addition to lenvatinib versus pembrolizumab plus lenvatinib.

Favezelimab is an immune checkpoint inhibitor targeting lymphocyte activation gene-3 or LAG-3, which is often co-expressed with PD-1 on T cells and NK cells. Inhibition of LAG-3 prevents its binding to MHC Class II and restores T-cell effector function. As shown earlier by Roy, activity of the combination of favezelimab and pembrolizumab demonstrated activity in patients with heavily pretreated microsatellite-stable colorectal cancer, which accounts for approximately 95% of metastatic colorectal cancers and which is resistant to monotherapy PD-1 inhibition. Historical data in MSS-CRC showed no responses to pembrolizumab monotherapy. There were also no responses to favezelimab monotherapy in a separate cohort of the current study.

Activity of the combination was enriched in a PD-L1 positive population, with an overall response rate of 11% and duration of response of 10.6 months. Additionally, previous work has suggested that PD-L1 expression is a negative prognostic factor in MSS colorectal cancer associated with

shortened survival. While in this study, patients' PD-L1-positive tumors treated with the combination of favezelimab and pembrolizumab had longer overall survival compared to patients with PD-L1 negative tumors.

Based on these promising data, a Phase III study of the co-formulation MK-4280A in MSS colorectal cancer will be initiated later this year. Signal detection work is ongoing in additional solid tumors and hematologic malignancies.

Finally, I will discuss MK-1026, a reversible noncovalent inhibitor of Bruton tyrosine kinase, part of the B cell receptor signaling cascade, which is critical to the proliferation and survival of B cells, including malignant B cells. Currently marketed BTK inhibitors are covalent inhibitors, which have demonstrated strong activity across a number of B cell malignancies, including chronic lymphocytic leukemia and mantle cell lymphoma. The most common mechanism of resistance to these covalent BTK inhibitors is a point mutation of cysteine to serine at amino acid 481 of BTK. MK-1026 does not interact with this amino acid and thus may retain activity even in the presence of this mutation.

Early data from a cohort of CLL patients With the C481S mutation in the Phase I for MK-1026 were presented at ASH in 2019 and showed responses in 8 of 9 or 89% of patients at a dose of 65 milligrams. These were heavily pretreated patients with median prior lines of therapy of 4. Responses were also seen in patients with Richter's transformation, an aggressive form of the disease associated with poor outcomes. Dose optimization work is currently ongoing, with registrational trials under development in parallel.

MK-1026 is part of our expanding portfolio in hematologic malignancies where we hope to build on the success of pembrolizumab in classic Hodgkin's lymphoma and primary mediastinal B cell lymphoma. Additionally, an antibody-drug conjugate targeting ROR1, which was acquired from VelosBio last year, has shown promising activity in B cell lymphomas and will be discussed in detail by Eric.

I'll now turn the presentation over to Eric for a review of our early-stage pipeline.

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**Eric Rubin**

Thanks, Vicki. So I'll again focus on the early pipeline. This pipeline includes more than 25 investigational agents, some of which are shown on this slide. They include immune agonists, including our CD27-agonist, MK-5890, which is in Phase II; as well as a systemically administered STING agonist, MK-2118 in Phase I. We also have a number of inhibitors of negative immune regulators beyond KEYTRUDA, these target pathways that are different than the pathway targeted by KEYTRUDA. The LAG-3, CTLA-4 and TIGIT compounds have already been discussed by Roy and Vicki. In addition, in this group, we have an anti-ILT-4 agent, which I'll describe in a minute as well as an ILT-3 antagonist in Phase I.

We're also focusing on personalized cancer treatments, such as our personalized cancer vaccine program, which is in Phase II, in collaboration with Moderna. We also have a KRAS vaccine being developed in partnership with Moderna, which is in Phase I, as well as small-molecule inhibitors of KRAS in partnership with Taiho/Astex.

We have a large and diverse effort targeting immune-suppressive tumor microenvironment, in addition to those described above. The HIF-2 alpha inhibitor and BTK inhibitor have already been described by Vicki. We also have AKT inhibitors, ERK inhibitors as well as ADC agents, which I'll describe shortly. We also have cytokine derivatives which are being developed in collaboration with Sutro in preclinical settings.

And then finally, recently, we've obtained cell-based therapies as well as T and NK cell engagers via partnerships with A2, Artiva, Janux and Dragonfly.

So now I would like to describe in more detail some of the early clinical data from 4 of our compounds, and I'll start with MK-4830, which is our ILT-4 antagonist. ILT-4 stands for immunoglobulin-like transcript 4. This is a pathway that's very promising, in that it targets myeloid-suppressive cells that are present in tumors, which are very important to potentially allowing the immune system to recognize tumors somewhat analogous to KEYTRUDA, but again in a very different pathway since we're targeting myeloid cells.

We showed early clinical data from this -- from the Phase I study from this compound at ESMO 2020. Those data are shown in the graph to the left, where we observed a response, both as monotherapy and several responses in combination with KEYTRUDA. Particularly notable were that many of these responses occurred in patients who had progressed on prior PD-1 therapy, and this would be unlikely to be expected to be the response

coming from KEYTRUDA alone. This compound is under broad evaluation in signal-finding studies in combination with KEYTRUDA in 9 different tumor types.

Next, I'll move to MK-2140, which is our antibody drug conjugate targeting ROR1. ROR1 stands for receptor orphan tyrosine kinase -- receptor tyrosine kinase-like orphan receptor. This is a protein which is expressed in embryogenesis. Expression is lost prior to birth, with reexpression in several tumors, including both hematologic and solid tumors. The figure to the rightmost part of this slide shows expression data for solid tumors, and you can see that there is expression across a broad variety of solid tumors. The graph in the middle shows early clinical data from a study in patients with mantle cell or diffuse large B cell lymphoma. And you can see impressive response rates for these patients.

The mantle cell -- this is a waterfall plot. The mantle cell data is shown in red, and the diffuse large B cell lymphoma is shown in blue. In addition to efforts to pursue this very promising data in hematologic malignancies, there is a Phase II -- ongoing Phase II in patients with advanced solid tumors.

Moving on to our next antibody drug conjugate. This is MK-6440. This targets LIV-1. LIV, as far as I can tell, that comes from the fact that the discoverers of this protein were based in Liverpool. This is a transmembrane protein with putative zinc transporter as well as metalloproteinase activity. And it is expressed in several solid tumors as shown in the RNA expression data on the right.

If we move to the next slide, this shows early clinical data both as monotherapy on the left in triple-negative breast cancer patients. You can see most patients had a reduction in tumor size. And more recent data, when combined with KEYTRUDA, is shown on the right, where you can see that greater than 90% of patients achieved tumor reduction in combination with KEYTRUDA.

Next, I would like to discuss our CD27 agonist. This is MK-5890. This is an antibody, when bound to CD27, results in T cell activation, including priming, differentiation, expansion and survival. We presented early clinical data from the Phase I at the SITC conference in 2019. Those data are shown here on the -- into 2 waterfall plots. The one in the middle is a monotherapy waterfall plot. You can see there is some monotherapy activity. And the one on the right shows the combination data with KEYTRUDA. We have signal-finding efforts in combination with KEYTRUDA in non-small cell lung cancer, triple-negative breast cancer and others.

Next, I would like to move on to our precision medicine efforts. We have an extensive history of pursuing efforts to identify patients who are most likely to benefit from our treatments. And these include PD-L1 expression with regard to KEYTRUDA and other immuno-oncology compounds. We had the first companion diagnostic approval for an immuno-oncology agent. This was for KEYTRUDA in non-small cell lung cancer, and it's turned out that PD-L1 expression has been important for identifying patients responsive to a number of cancer patients with KEYTRUDA, including gastric, cervical, bladder, esophageal and the head and neck cancers.

We've also found that there's another access that's important to immune-oncology response. This is related to increased antigenicity due to high DNA mutation load. We had the first approval in this effort based on a tissue-agnostic approval, where we were initially in collaboration with Johns Hopkins investigators. We identified that patients with MSI high cancers were highly responsive to KEYTRUDA and then this extended to colon cancer as well as others.

More recently, we had a second approval based on this concept. MSI high is only one way to obtain a high DNA mutational load. And through a study known as KEYNOTE-158 as well as others, we've shown that patients who have a high mutational burden are highly responsive to KEYTRUDA monotherapy. This resulted in an accelerated approval by FDA and as well as an approval of associated companion diagnostic.

We also have efforts related to our PARP inhibitor, Lynparza, where we're developing biomarkers related to identification of patients with defects in the homologous recombination pathway. These include both BRCA mutations as well as other mutations in DNA repair proteins or other methods to identify patients who are likely to be responsive to Lynparza.

And then finally, we have a robust exploratory biomarker effort involving our early pipeline. This includes immunochemistry evaluations for our TIGIT, ILT-4, ROR1, LIV-1 targets as well as our TriNKET program, in collaboration with Dragonfly. And we're pursuing exploratory biomarkers in our BTK and KRAS targeting programs.

And I'll just note, as commented on the bottom, that we have a very careful path to identifying predictive biomarkers that are based upon strong biological hypotheses and rigorous statistical approaches that identify biomarker cutoffs defined prospectively based on threshold analyses and independent training sets.

And this last slide just notes that some of our recent approvals in 2020 that -- where there were 2 new biomarker-driven approvals, one was the TMB high approval that I mentioned previously, you can see the response rates that's seen in the KEYNOTE-158 pan-tumor study of 30% compared to 6.7% of patients who are not TMB high. And then we also had an approval in first-line MSI high colorectal cancer based on robust PFS results from KEYNOTE-177, with a hazard ratio of 0.6.

So I would now like to pass the presentation on to Jannie for a commercial update.

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**Jannie Oosthuizen**

Thank you, Eric. As Dean mentioned in the opening, I will highlight how we believe the data and our ongoing effort to address unmet need will continue to drive significant commercial opportunity and growth for Merck.

Despite the significant advances in cancer care over the past decade, unmet needs remain high and cancer patients continue to need innovation. The science in oncology continues to accelerate, and MRL has been and continues to be a key contributor to that accelerating science.

KEYTRUDA already became a foundational cancer treatment in a number of tumor types. But as you saw from our MRL colleagues, we are not stopping there. We are deepening responses with combinations, expanding our portfolio of products and making a significant move into early-stage treatment in order to address these unmet needs and attempt to deliver increasingly better outcomes. At the same time, the landscape with respect to access and pricing continues to change. And the need to demonstrate value through clinical data and improve patient benefit over standard of care is becoming more demanding than ever. As a commercial organization, we continue to be ready to execute on these opportunities, with robust data from MRL and a sense of urgency.

We are driving global leadership across a broad portfolio of commercial assets. As I said earlier, KEYTRUDA is in a leadership position as a foundational cancer treatment, and Lynparza is the market-leading PARP inhibitor. Lenvima, as a broad-based TKI, continues to add significantly to our portfolio, including in combination with KEYTRUDA. And we are excited about the potential of our recently added TUKYSA, a highly selective small-molecule TKI. In total, we have over 40 approved indications in the U.S. across 20 tumor types, including 2 tumor-agnostic approvals that Eric spoke about.

We are well positioned for continued success as we roll out new indications and combinations move to earlier lines of therapy and launch new assets. One of our new assets to be launched in 2021 is belzutifan, and Vicki touched comprehensively on this product. As Vicki mentioned, we are looking forward to bringing belzutifan to a small population of patients with VHL-associated renal cell carcinoma in September this year. Our expectation is for belzutifan to become a blockbuster drug in the medium term, with growth opportunities in RCC and potentially beyond. This asset was the result of business development where we saw an opportunity in early stages, required this compound and quickly developed it for this first indication.

We continue to be very pleased with our collaboration and partnership with AstraZeneca. Lynparza has demonstrated improved patient benefit with approvals in 7 indications in the U.S. across 4 different tumor types. The positive data from OlympiA in early-stage breast cancer is already encouraging -- is really encouraging as we extend the benefits and reach of Lynparza, and we hope to be able to add this adjuvant indication in the near future. We have a comprehensive development plan underway studying Lynparza as monotherapy and in combination with KEYTRUDA, which will position us well for significant growth going forward.

Our partnership with Eisai is also proving to be very successful from both a commercial and development perspective, with a number of approved Lenvima indications in markets worldwide already. In addition, we have 20 combination studies with KEYTRUDA across 14 tumor types ongoing. In the near term, we expect to expand our indications with launches in first-line renal cell carcinoma and in second-line endometrial carcinoma to even more patients based on practice-changing data presented earlier this year. We expect continuing growth of Lenvima as positive data reads out.

An important early benefit from both partnerships was that it helped us move into new areas and establish an early footing in new customer settings such as urology and women's cancers. This continues to serve us well as we build out a broad GU and women's cancer presence and portfolio.

Early-stage treatment represents a critical opportunity where we believe Merck is uniquely positioned to win. Early-stage treatment will contribute to more than half of KEYTRUDA's growth over the next 5 years. We already have 2 early-stage indications, adjuvant melanoma and non-muscle invasive bladder cancer approved in the U.S. And our vast early-stage clinical program covers multiple solid tumor indications as you will see on the next slide.

Merck is well positioned in key tumor types with more than 20 Phase III studies underway with some already approved or reading out. As Roy highlighted earlier, we've demonstrated improved patient benefits in adjuvant renal cell carcinoma based on the KEYNOTE-564 data presented yesterday at ASCO, and we have shown positive top line results from KEYNOTE-522 with event-free survival in new adjuvant and adjuvant triple-negative breast cancer. We are looking forward to more positive results in multiple tumors including lung, stage 2 melanoma, head and neck, bladder, gastric, and esophageal cancers.

Merck also has the broadest clinical development program in early bladder cancer with the approval of KEYTRUDA already in non-muscle invasive bladder cancer and multiple ongoing trials in muscle-invasive bladder cancer. We have a significant opportunity for KEYTRUDA to lead I-O in the early treatment setting as the first entrant to market in most of these tumors, further building on our already strong presence and leadership in metastatic disease.

As Dean mentioned earlier, our aggressive investment and broad clinical program are expected to result in more than 90 potential approvals between now and 2020 with over 50 approvals already by 2025. A large portion of these approvals include new assets, many of which we expect to co-formulate with KEYTRUDA. These indications and treatments are designed to reach more patients and improve on current standard of care, providing important patient outcomes benefit, including convenience.

Importantly, there is also the potential to benefit health systems and providers with respect to both access and infusion center capacity as was proven with the great success of KEYTRUDA Q6W in the past year. The co-formulations, should they read out positively, can potentially extend portions of the KEYTRUDA franchise well beyond 2028.

To conclude my part of the presentation, Merck's incredible clinical and commercial execution has led us to become a foundational player in oncology today with clear leadership in I-O. We fully expect the strong execution to continue and for Merck to be the leading oncology player by 2026. Our diversified approach across earlier lines of therapy, multiple combinations and co-formulations as well as new assets will contribute to a tripling of indications in the next 8 years. Building on our leadership in lung, these launches will drive significant growth, led by early-stage treatment but also areas such as GU where we will see significant growth.

In summary, we are very confident in our positioning in oncology and the substantial growth ahead over the next several years. Our strong presence in oncology is likely to extend well into the next decade.

I will now turn the call back to Dean.

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**Dean Y. Li** - *Merck & Co., Inc. - EVP*

Thank you, Jannie. You've now heard from my colleagues on how we are continuing to establish KEYTRUDA as a foundational treatment by expanding to additional tumor types in earlier stages of disease. Importantly, we are leveraging the data and insights gained from KEYTRUDA, Lynparza and Lenvima to build and advance a growing portfolio of innovative early- and late-stage oncology assets obtained through acquisitions, partnerships and our own discovery programs. And Merck's data presentation at ASCO reinforces how we are executing on this strategy. I'm confident our company is uniquely positioned to have a sustained and enduring beneficial impact in oncology through this decade and into the next.

Thank you for your attention. Now we look forward to taking your questions. Peter, do you want to kick it off?

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

Yes. Lara, can we queue up the questions, please?

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## QUESTIONS AND ANSWERS

**Operator**

(Operator Instructions) Your first question will come from the line of Daina Graybosch from SVB Leerink.

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

I wonder if you could talk about maybe an observation and then a question. We see some different approaches at some of your second-generation combinations, let's say TIGIT, LAG, len and ILT-4, where some seem more narrow, some seem more broad. Now that there is, I'd say, some pretty good proof-of-concept data for at least all of these or part of these, can you help us understand what's guiding your strategy as you take these forward into registration trials? What's going to really lead to success? Is it indication? Is it biomarker? Is it first to launch?

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

Roy, would you like to lead the response to that question?

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**Roy D. Baynes** - *Merck & Co., Inc. - Chief Medical Officer*

Sure. Well, as you've seen, we have a pretty extensive array of assets to develop, and we can take a broad-based approach to everything. So we're trying to do this in a very informed way. Some of this is informed by biologic plausibility. Some of it is informed by informative precision medicine tools. And Eric may want to embellish on that in just a moment. And then some of it is led by clinical data, and a lot of the clinical data comes out of signal finding experiments.

And when we find a signal, we are apt to double down on that signal, particularly if it's in a tumor type of high unmet medical need and meaningful patient numbers. And so that's sort of the general approach we take. I think also, we're at a moment in time and clearly, depending on additional signals coming, you will see broadening out of some of these approaches. And Eric, I don't know if you want to embellish at all on the precision medicine tools.

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**Eric Rubin**

Thanks, Roy. Yes. So as I mentioned, all of our programs, we include rigorous predictive biomarker where this starts preclinically, extends into our Phase Is and if needed, will progress into Phase II or registrational intent studies. And I think as we said, again, we're fortunate to have a number of compounds in the early pipeline. We can't study every tumor type with every compound, but I think we've tried to be efficient in this and base our decisions on emerging clinical data. And of course, this is what we did early on with the KEYTRUDA program where our initial Phase I became a 1,200-patient study based on emerging clinical data.

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**Dean Y. Li** - *Merck & Co., Inc. - EVP*

Yes. This is Dean. I would just add that when we're talking about plausibility, precision clinical data, signal finding, that focuses both on our internal data and programs, but we are very aware and we follow very closely those done by other companies. And we pull it together to see where is the place that we should invest in fastest and quickest to get the signals and then to broaden as appropriate.

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**Operator**

Your next question comes from the line of Steve Scala from Cowen.

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

A couple of questions. How does Merck anticipate Bristol's relatlimab plus Opdivo combination impacting KEYTRUDA monotherapy use in melanoma. We estimate KEYTRUDA sales in melanoma at about $2 billion or about 12% of KEYTRUDA sales, so it's a sizable portion of sales at risk.

And secondly, a little bit bigger picture. But Dean, you noted the clinical trial activity for KEYTRUDA and the fact that you have 25 novel mechanisms in development, which collectively fortify this enduring success that you foresee. But in a recent sell-side meeting, when Rob was asked about the pipeline, he mentioned several therapeutic categories but not oncology. So what percent of Merck clinical trial candidates and R&D spend is devoted to oncology now? How do you see that trending over time? And can you tell us whether or not you have other R&D programs that also could lead to enduring success?

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

First part of the question on the melanoma market, maybe a combination of Eric and Jannie with respect to Bristol's program.

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**Jannie Oosthuizen**

Yes. So I'll just start. I think in terms of how this is going to play out in first line, I think we need to see how the data ultimately comes through in terms of whether they're going to have overall survival. We know that current treatments have a strong data package within the first-line setting. So I think it's a question of how the data is going to come through and how positions will look at that in relation to current standard of care in the first line.

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

Anything to add, Vicki or Eric? Yes. Roy?

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**Roy D. Baynes** - *Merck & Co., Inc. - Chief Medical Officer*

Yes. I mean just for clarity, we think of melanoma in a number of different categories. So we think of obviously adjuvant melanoma, we think of metastatic melanoma. We think of melanoma with unusual characteristics such as brain metastases and other presentations.

In the adjuvant setting, we believe we have an extraordinarily strong package. 054 and 053 together are really defining that space, and we are expecting additional readouts in earlier stages of disease such as stage 2 disease, and that trial is ongoing at this point. So we are actually very excited about our prospects in the adjuvant setting.

I think the question of the combinations in the adjuvant setting, you're probably aware of a recent failed trial where indeed I-O, I-O combo really added nothing. And I think in the combination setting, I think you're always balancing efficacy and toxicity. And I think monotherapy is well

established as an effective metastatic treatment and has a very favorable benefit/risk profile. Just to be clear, we have a LAG-3 as well, and if we see compelling data, there's every reason that we might well advance a program of our LAG-3 together with pembrolizumab.

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**Dean Y. Li** - *Merck & Co., Inc. - EVP*

Yes. In terms -- this is Dean. In terms of the broader questions, especially in relationship to the comment made about Rob's discussion previously, I think Rob was trying to emphasize the non-oncology programs more than not touching on them as a formal sort of statement of importance. The oncology portfolio, as you've seen, is extremely robust. If you just take the KEYTRUDA, Lenvima and Lynparza, you take the different compounds that we've talked about, those are all substantial investments that are being made and substantial investments that have been made. And if you look out between '21 and '23, '24, those are important readouts for us to obtain and to continue to invest.

When we speak about other non-oncology sort of assets, I think that's what Rob was trying to sort of emphasize that we have opportunities outside of oncology to make important impacts. We've talked about vericiguat. We've talked about V114, dengue, inhaled sGC, the recent sort of acquisition of Pandion's immunology asset. But probably one of the things that we are extremely excited relates to islatravir. We have 2 Phase III trials starting for PrEP. We have the collaboration with Gilead as we look for combinations both internal with our MK-8507 and with other partners, lenacapavir, in relationships to treatment, which is the vast majority of the market of HIV at this time.

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**Operator**

Your next question comes from the line of Mara Goldstein from Mizuho.

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**Mara Goldstein** - *Mizuho Securities USA LLC, Research Division - MD of Equity Research Department*

Just first, a bit of a clarification on I think the last slide that was up in Jannie's presentation, you spoke to leading oncology company by 2026 and a number of lines on that graph. What do those lines actually represent? And then secondarily, I'm wondering if you can talk a little bit about Lenvima's development in light of the prioritization around combinations and in light of the LOE this decade.

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**Jannie Oosthuizen**

Yes. So let me clarify. The last slide was the Evaluate Pharma prognosis of how the oncology market is going to play out by 2026, and it shows Merck rising to the top by 2026.

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

Yes. Each of those lines represent other companies.

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**Jannie Oosthuizen**

Yes, each of the lines below that, yes, represent our competitors.

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

A question on Lenvima.

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**Roy D. Baynes** - *Merck & Co., Inc. - Chief Medical Officer*

Sure. And I think what you're seeing is lenvatinib combines very nicely with pembrolizumab. We have already read our 2 Phase III trials where, indeed, we do believe these will be practice changing. And certainly, we expect a number of more readouts over the next months and years. And the LOE statement is correct, but having said that, there's tremendous benefit of this combination. And obviously, that LOE is still a good few years off. In addition, KEYTRUDA continues to be a key component of that combination even once lenvatinib gets past LOE.

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**Operator**

Your next question will come from the line of Geoff Meacham from Bank of America.

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**Geoffrey Christopher Meacham** - *BofA Securities, Research Division - Research Analyst*

I want to talk a little bit about RCC. When you think about putting KEYNOTE-564 into practice, how do you see the share shaking out downstream? I was just curious if maybe there are commercial lessons to be learned about what impact adjuvant I-O use has or had in melanoma demand or share later on in metastatic setting, maybe what that could do for in the RCC market.

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

Roy, do you want to start?

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**Roy D. Baynes** - *Merck & Co., Inc. - Chief Medical Officer*

Sure. So as we look at RCC, each tumor type is a little different. So when we think about, for example, non-small cell lung cancer, we see a circumstance where indeed a very large proportion of patients present with advanced disease and metastatic disease and a smaller percentage present as early-stage inoperable disease. So the chances are, these are going to behave as relatively distinct populations. I think in the renal cell setting, a proportion of patients do start off with early-stage disease, surgically treated and a proportion will recur. As we said, about 50% of patients with high-risk renal cancer treated surgically will recur. Those clearly will be affected by the adjuvant use of I-O drugs.

What's not known is what is the optimal treatment for patients who have recurred after adjuvant I-O. I will share with you that, in a number of trials where we are exploring I-O combinations, we see a proportion of patients who have robust responses to the same I-O agent combined with an alternate partner. In addition, for patients who had been treated with an I-O drug and were followed for, let's say, 2 years in the metastatic setting and then come off treatment, a proportion of those when they recur, actually have a second response to the same I-O drug. So it's not a mutually exclusive equation, but it does mean that there's a lot of development work to be done to actually optimize the salvage therapies in patients who have failed an I-O drug.

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**Operator**

Your next question will come from the line of Louise Chen from Cantor.

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

So first question I have for you is how do you see the standard of care for renal cell carcinoma evolving. How do you think about the sequencing of potential new treatments? And where would belzutifan fit into the treatment paradigm if it's approved?

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

Great. Roy?

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**Roy D. Baynes** - *Merck & Co., Inc. - Chief Medical Officer*

So as you have seen, we have a formidable array of assets to address renal cell cancer. The combination of TKI together with pembrolizumab, has turned out to be a very active and very important treatment in the advanced disease setting in frontline treatment. The adjuvant trial clearly marks monotherapy as an important component of frontline treatment. Belzutifan, as you've heard from Vicki and as we have shown, is very active in the VHL setting. Now the reason that is so important to know is that the majority of patients with sporadic renal cell cancer actually have dysregulated VHL apparatus. It's as if they had VHL disease in many ways.

And so we do believe and we've already got Phase II data to show that belzutifan is a meaningful salvage therapy after I-O and TKI failures. However, we think that belzutifan is going to be more than just a salvage treatment. There's every reason to believe that it will combine quite well potentially with an I-O drug. Remember, one of the major effects of belzutifan is an orthogonal attack on the angiogenesis process. And so we do think this will be a meaningful salvage therapy, and we will explore it extensively in the frontline treatment of metastatic disease and potentially once we have pembrolizumab bedded down as an adjuvant treatment as a potential combination in the adjuvant setting.

So there's a broad array of possibilities there. And we have now got really a very strong arsenal here, including VEGF-targeted agents HIF-1 -- HIF-2 alpha targeted agents as well as meaningful I-O therapies.

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**Vicki Goodman**

Wait, would you like me to add some -- okay. So maybe I'll comment on the 3 Phase III studies that we have for belzutifan in the advanced renal cell carcinoma setting. So the first is a third-line trial of belzutifan versus everolimus. So these are in patients who've been previously treated with both I-O as well as a TKI. We have a second-line trial in combination with lenvatinib. So this is, again, a combination that attacks angiogenesis from 2 angles versus cabozantinib, so that's a second-line trial. And finally, there is a first-line combination with pembrolizumab and lenvatinib versus the pembrolizumab plus lenvatinib combination from KEYNOTE-581. So taking a really broad approach to looking at belzutifan, both as a monotherapy and in combination in advanced renal cell carcinoma and as Roy mentioned, there are opportunities there to take that into earlier stages of disease as well.

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**Operator**

Your next question will come from the line of Terence Flynn from Goldman Sachs.

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**Terence C. Flynn** - *Goldman Sachs Group, Inc., Research Division - MD*

Great. I just had one -- another one on KEYTRUDA in adjuvant RCC. I was wondering if you'll need overall survival data to file on. And then I was looking at -- it looks like the current rate of adjuvant treatment for RCC is about 10% to 15% of patients. So just wondering where can that go over time. I think melanoma is up to maybe 70% now or so. Is that the right way to think about it? Or is it likely to be somewhat different?

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

Roy?

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**Roy D. Baynes** - *Merck & Co., Inc. - Chief Medical Officer*

So when we think about adjuvant renal cell treatment, up until now, there have been very few effective adjuvant therapies. There's really only been one positive trial. The drug did get approved. But having said that, it is not widely used. And indeed, there's been a recognition up until now that there's equipoise in this area around doing placebo-controlled trials. So the rate of use in the adjuvant setting is extremely low because there's been very little effect of therapy.

We do believe that pembrolizumab, which is generally well tolerated, adverse event profile is well understood and well managed, will be a very significant addition to the adjuvant armamentarium. And we do think that, over time, we will see a pretty significant ramp in the adjuvant treatment of this disease.

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

And the second part of the question, Jannie?

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**Jannie Oosthuizen**

Yes, I can add. I agree with Roy. I think the diagnosis in RCC happens early, so about 75% of patients are diagnosed in the early setting. To Roy's point, I think with the emergence of effective therapies, it's going to be interesting to see how many patients are treated.

In terms of the population that we can treat with 564, it probably equates to what we are treating in the metastatic setting just given the intermediate and high-risk population. But it is a meaningful opportunity, and over time, we will have to see, as an effective therapy takes hold, how physicians adopt it.

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**Operator**

Your next question will come from the line of Seamus Fernandez from Guggenheim.

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

So I guess the first question is on LAG-3 with pembrolizumab. It looks like on the basis of the relatlimab data that perhaps LAG-3 isn't necessarily a positive predictive biomarker but a negative prognostic biomarker. Just interested to get your thoughts on the value of LAG-3 as a biomarker in Merck's end in particular and if you see a future for LAG-3 as a biomarker in that regard.

The separate question is really on your ILT-4. Just wanted to get a better sense of your development plans for ILT-4. And when we're likely to see the next sort of mission-critical data set?

And then the final question is for Dean. Dean, I think on a previous call, you've been asked about the timing of when you expect meaningful clinical pivotal data to start emerging from the oncology combination pipeline. I think you had said that your expectations were for combination with KEYTRUDA, we might start to really see data in 2025. Is that still the time line for us to think about? Or should we be thinking about clinical data that really will raise the conviction level inside Merck to a different threshold and perhaps with investors sooner than that?

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

Thanks, Seamus. I think the first 2 questions are for Eric.

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**Eric Rubin**

Yes, Seamus, so we've looked -- in our program, we've looked carefully at sort of all the I-O biomarkers that we've mentioned. So PD-L1, LAG-3, TMB. We have a gene expression inflammatory signature, and we have -- we found that PD-L1 does correlate with outcomes in the combination. LAG-3 does not seem to add to that. So that's our current data from what we have.

With regard to ILT-4, I think, as I mentioned, we have -- we're investigating this in signal finding across multiple different tumor types. These are accruing rapidly. Perhaps next year, we'll be presenting the next set of data at a meeting.

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**Dean Y. Li** - *Merck & Co., Inc. - EVP*

In relationship to the comments that I made previously, for me, looking at co-formulation especially with KEYTRUDA and especially with other I-O agents such as TIGIT, CTLA-4, LAG-3, the start of when we do the Phase III trials gives you a general sense of when we might be able to see data that could lead to approval. So that's what I was sort of referencing previously.

And as we've discussed here, there is the start of a series of Phase III trials in relationships, so our conviction is we want to set the Phase III trials. And if they read out positive, then there's a general sense, that's why I gave you the timing of '24, '25, '26 in that range, depending on -- these are event-driven trials that, that would be when one would begin to see not conviction to go to Phase III but the potential results from the Phase III that could lead to approvals of those goal formulations.

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**Operator**

Your next question comes from the line of Chris Schott from JPMorgan.

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

I guess just one question, bigger picture on the co-formulation, how you think about pricing. Should we think about these as assets that would be priced at a significant premium to KEYTRUDA. So basically, you priced them almost as 2 -- you would 2 novel agents? Or do we think about these being priced at a more modest increase over KEYTRUDA with the benefit of Merck from these being more the extended life they bring to the KEYTRUDA franchise?

And then my second question was just on the LAG-3 and this MSS CRC market. Can you just elaborate a little bit more on the Phase III program? So specifically, I guess, how late of line of therapy you're targeting? And maybe just help put that 11% response rate you saw from the Phase I into context as we think about the hurdles for the Phase III program?

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**Jannie Oosthuizen**

Yes. So I'll take the one on pricing. I think it is a bit early to go into the price potential of these combinations. I think prior to 2028, it is purely combinations, right? So it's co-formulated. So from an access and pricing perspective, I think there's a good case to be made that it's a combination of the 2 products. Beyond that, we need to look at -- we have work underway in terms of determining the price outlook into the longer term.

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

Great. Thank you. Vicki?

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**Vicki Goodman**

And for LAG-3 in MSS CRC, yes, so the initial registration trial, we haven't announced the details yet, but I will share that this will be in a later line of therapy where you're looking at a lower bar with respect to both response and overall survival. And we believe and are confident based on our data that in that setting, where the standard of care is poor and there remains a big unmet need, that we have an opportunity to show benefit.

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**Operator**

We do have a follow-up question, comes from the line of Mara Goldstein from Mizuho.

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**Mara Goldstein** - *Mizuho Securities USA LLC, Research Division - MD of Equity Research Department*

I appreciate that. I just -- I had a follow-up question just on belzutifan. You had mentioned other indications outside of renal. And I was curious as to what the development plans there -- were there, particularly having mentioned pancreatic cancer.

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**Vicki Goodman**

I think it was prostate cancer actually that was mentioned. So yes, so belzutifan, we see activity, as was mentioned in VHL-associated renal cell carcinoma, and that's really a model system for clear cell renal cell carcinoma. And that's why, when we're looking more broadly right now, we're looking specifically at renal cell carcinoma.

I think based on the mechanism of action and the fact that ultimately you're targeting the angiogenesis and survival pathways, there are opportunities beyond that in VEGF-responsive tumors. And so we'll continue to look for signals in some of those tumors as well, maybe perhaps in combination with lenvatinib and other agents. And so there are opportunities for additional signal finding work, and then further registrational trials will be informed by the signal finding work that we'll do -- we are doing.

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

Thank you, Vicki, and thank you, Mara. And thank you, everybody, for joining us this evening. We appreciate your time and your attention and your questions. And we look forward to any follow-ups that you might have. Reach out at any time. Thank you so much.

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