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OVERVIEW:

Company Summary

LSEG DATA & ANALYTICS

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PRESENTATION

Operator

Thank you for standing by. Welcome to the Merck & Co., Inc. Rahway, New Jersey, U.S.A. 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, Senior Vice President, Investor Relations. Sir, you may begin.

Peter Dannenbaum - *Merck & Co., Inc. - Senior Vice President, Investor Relations*

Thank you, Ivy, and good evening, everyone. Welcome to Merck's investor event at the American Society of Clinical Oncology Annual Meeting. Thank you to all of you who've made the effort to be with us here in Chicago. It's great to see such a great crowd here tonight, and thank you for those that are tuning in via the webcast.

So we're 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 and has been posted to the Investor Relations section of Merck's website.

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 our Company'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 2025 10-K, which identifies certain risk factors and cautionary statements.

So our agenda tonight will start with Dr. Dean Li, President, Merck Research Laboratories, who will make a few opening remarks. Dr. Marjorie Green, Senior Vice President and Head of Oncology, Global Clinical Development, will provide an overview of our oncology strategy and key progress across the portfolio, including important clinical data updates.

Next, Jannie Oosthuizen, Executive Vice President and President, Oncology and MSD International will speak to the commercial landscape and the opportunity we see to further impact patient lives.

Dean will then provide closing remarks before we get to Q&A. Sophie Opdyke is sitting here in the front row, Senior Vice President of Global Oncology Marketing, and she will also be available for Q&A.

So with that, I'd like to turn it over to Dean.

Dean Y. Li, M.D., Ph.D. - *Merck & Co., Inc. - Executive Vice President and President, Merck Research Laboratories*

Good evening. It's a pleasure to see so many of you here in Chicago.

One of the things, I think, is important is we're trying to create a cadence of what our strategy is and try to define what it is and hold ourselves to be predictable in saying that in 2021, we outlined two clear objectives: to sustain durable leadership in oncology. We wanted to maximize the positive impact of KEYTRUDA, especially in earlier stages of disease, and to diversify our pipeline with novel mechanisms.

And then since then, we have made steady and important progress in demonstrating the benefit of KEYTRUDA in improving patient outcomes, especially in the earlier-stage setting.

Last year, we also introduced KEYTRUDA QLEX, a subcutaneous injection of pembrolizumab plus berahyaluronidase alfa, allowing the administration in as little as one minute when given every three weeks. And we have leveraged the data and insights gained from KEYTRUDA to advance a broad and diverse pipeline of innovative candidates and novel mechanism of actions.

And I think Marjorie will speak to a few of them, but we use our experience with KEYTRUDA and what it can combine with in how we look at these novel mechanism of actions. And we also look where KEYTRUDA doesn't work so well and where we want new mechanism of actions as well.

And then over the course of the last few years, these two objectives have been our guiding principles. And this evening, you will see some significant progress we have made in executing against them. So let me put our progress in context because where KEYTRUDA goes allows us to figure out where other things should go and gives us a leveraging point in relationship than that.

So KEYTRUDA has now received FDA approvals for 44 indications across 19 tumor types as well as two tumor-agnostic approvals, and clinical programs continue to generate evidence with the potential to further transform cancer care.

In 2021, we also felt that our ambition would be that 25 percent of KEYTRUDA sales would transition to go much more in the earlier stage indication by the end of 2025, and we've achieved that ambition. That ambition is important as we think in the future about our pipeline, but also setting up were subcut KEYTRUDA can go -- KEYTRUDA QLEX can go.

And so today, KEYTRUDA-based regimens have received FDA approval for 11 indications in the earlier setting, of which six studies have demonstrated an overall survival benefit; the gold standard for oncology trials.

So KEYTRUDA continues to raise the bar in treating earlier stages of disease and improving patient outcomes and laying a roadmap for us to follow. We have advanced our foundational position with KEYTRUDA to create a diverse pipeline by executing on three pillars that we think is important.

Immuno-oncology, and you've seen KEYTRUDA, we've talked about KEYTRUDA QLEX, but it is around PD-1 VEGF. It is around INT as well. Precision molecular targeting that many -- some of the programs that Marjorie -- and also a very robust tissue targeting candidates in the ADCs, both internally but also with robust partnerships with Daiichi Sankyo and especially with QLEX.

In total, we now have approximately 60 Phase 3 oncology trials, of which 40 are across novel pipeline candidates including our suite of antibody drug conjugates, T cell engagers, small molecules, and individualized neoantigen therapy. These diverse candidates are being developed as monotherapy as well as in combination with KEYTRUDA or KEYTRUDA QLEX.

And the culmination of the late-phase studies is a result of years of disciplined pipeline diversification, both through internal discovery and strategic business development. We believe that we are well positioned to deliver a steady stream or cadence of meaningful data readout over the coming years and further the impact on patients with cancer.

And with that, I will turn it over to Marjorie.

Marjorie Green - *Merck & Co., Inc. - Senior Vice President, Head of Oncology, Global Clinical Development*

Thank you so much, Dean.

If you think about the portfolio, and Dean set up how we think about drug development and the assets in our organization, we think about three pillars of biology. And we do that because of the underlying mechanisms of growth and resistance of different cancers and being able to have drugs that can target specific biological pillars, and they can be combined together.

So our immuno-oncology medicines are designed to stimulate anticancer immune responses. These include KEYTRUDA QLEX, our investigational INT candidate, and our PD-1 VEGF bispecific.

Precision-targeting agents are designed to impact pathways that can derive cancer growth. This includes calderasib, our investigational KRAS G12C inhibitor, which recently received breakthrough therapy designation in the first-line non-small cell lung cancer setting; as well as several agents from our growing hematologic portfolio, and which I'll further touch upon later in the presentation.

Finally, tissue targeting, which includes antibody drug conjugates as well as T cell engagers. These are designed to target chemotherapy and immune cell activation to tumors while attempting to mitigate effects on normal tissues.

The reason we've organized around these goes directly to our strategy. And so to have the maximum benefit for patients and meeting the needs of these patients as well as clinicians and society is we know that the best outcomes in oncology, how and when you give multiple drugs together or are the different mechanisms resistance for the heterogeneity that exists in most cancers combinations have had the best outcomes long term. And we've seen that for many of our KEYTRUDA studies with multiple diseases and multiple combinations. And so we want multiple mechanisms to have the best benefit.

We also want to develop agents, therefore, that have single agent activity that are active in and of themselves and that are combinable because that will give us the best opportunity to help the most patients with a specific kind of malignancy or a subtype of a malignancy. And we can have diversified regimens also that potentially can go across multiple tumor types depending upon the targets and the mechanisms of action.

We also want to improve the therapeutic index of our medications. That is to be able to help a physician and a patient understand for a specific tumor that a person might have, is there a biomarker that could predict benefit of therapy because every time someone is treated, a physician can tell someone, we'll hear the odds that someone like you might benefit from a therapy. But knowing for that individual sitting in the chair in front of you, it's often very difficult.

We're talking about statistics. And as a person who sees a physician, that's really uncomfortable place to be. So if we can develop targeted therapy diagnostics, that will be really helpful to find those patients most likely to respond.

And critically, we want to bring these drugs into earlier stages of disease, as Dean talked about with what we've done with KEYTRUDA. And it's because we can have the greatest impact there. We can help the most number of people with cancer if we can treat the disease as early as possible, whether it is in the first line or second line setting in a metastatic disease or if it's in the potentially curative setting in the adjuvant or perioperative space.

So we take these three pillars, and we created diversified regimens that can be delivered generally across multiple tumor types. And so I'm going to start the update with one of the drugs that can do just what I talked about, which is sac-TMT.

It is one of our broadest programs in our pipeline. This is an antibody drug conjugate that we brought in through our partnership with Kelun Biotech. It's a differentiated TROP-2 antibody drug conjugate with a belotecan-derived topoisomerase I inhibitor payload.

What we're particularly excited about is the bifunctional linker technology that's proprietary and is quite unique for the TROP2 ADCs that are currently in clinical studies. This linker is designed with the intent to maximize payload delivery due to its very stable irreversible connection to the antibody.

This is intended to prevent the payload for breaking off the circulation. There is a pH-sensitive connection that ensures intracellular payload release in tumor cells. There also is the allowance of the structure for bystander effect.

The stability of the linker also enables a drug-to-antibody ratio of somewhere between 7:8, we say 7:4 to be very precise. But it's a very -- for the stability of the linker, this is a very high DAR when you look at other antibody drug conjugates. And so based upon its design and the compelling data generated so far, by our partners at Kelun, this has the potential to be a cornerstone antibody drug conjugate across a variety of different cancers.

So one such data set was the data you've seen at ASCO this year from OptiTROP-Lung05. This is a Phase 3 study conducted by our partners in China. And the study enrolled people who have non-small cell lung cancer, it could have been an adenocarcinoma or squamous cell carcinoma, with expression of PD-L1, 1 percent or higher, locally advanced, better as inoperable or metastatic non-small cell disease.

These are people who had no prior systemic antitumor therapy, and they were randomized to receive monotherapy pembrolizumab or the combination of sac-TMT and pembrolizumab. The combination of sac-TMT and pembrolizumab provided a clinically meaningful and statistically significant improvement in progression-free survival by blinded investigator, blinded central radiology review in the overall study population.

This benefit was very consistent across subgroups. We're including those who had PD-L1 high expression, those with lower PD-L1 expression, squamous histology, non-squamous histology, age across all of the different categories, there was consistent benefit.

And the intent-to-treat population, noting that this is very immature follow-up at this time, there is an OS trend observed noting again, it's very immature. And so no definitive conclusions can be made about that data. But it's really exciting. It is.

And particularly, we consider other Phase 3 data sets coming out of China and similar populations. It helps to demonstrate the promise of sac-TMT combined with pembrolizumab in our global TroFuse program, particularly TroFuse-007. We are conducting for participants who have non-small cell lung cancer whose tumors have a TPS score of greater than 50 percent.

We have other global Phase 3 studies in non-small cell lung cancer underway. The OptiTROP-Lung05 study adds to the growing body of data generated by Kelun Phase 3 studies. You're now seeing multiple proof points across well-conducted, randomized clinical data sets in multiple tumor types, including lung and in breast cancer.

Most recently, Kelun announced positive results from OptiTROP-Breast03 study in the first-line triple receptor negative breast cancer space a few weeks ago. Many of these proof points tie directly into studies that we have ongoing in our global TroFuse program. It is this collaboration we have a Kelun that allows us to expand and go into so many tumor types with confidence.

Our TroFuse development program is broad, and we think it's differentiated. TROP-2 is highly expressed across multiple tumor types. And we've designed Phase 3 studies in tumors where there's an opportunity for us to meaningfully impact cancer care either with a differentiated development profile or where we can be a first mover. As you see, we are advancing studies across gynecologic, breast, lung, gastric, and bladder cancer spanning from mid to late line in some settings, but mostly in the earlier stages of disease.

We are also pursuing maintenance regimens in several of our studies. And many of these indications, these are first-mover opportunities in the way that we have developed our Phase 3 program.

In keeping with our strategy to improve the therapeutic index of our assets, we have a robust biomarker strategy in place for sac-TMT. We have a broad development plan; not every tumor may benefit from enrichment. The data that we've seen with our biomarker development conducted during our extensive Phase 1/2 studies in collaboration with our partners in China has guided the implementation of biomarkers into our Phase 3 program.

I'm very pleased to share that TroFuse-005 is the first positive global Phase 3 for sac-TMT that has been conducted by Merck. This study demonstrated a statistically significant and clinically meaningful improvement in both progression-free and overall survival of certain patients with endometrial cancer.

This is the first TROP2 ADC to show improvement in overall survival and progression-free survival compared with chemotherapy in certain patients with advanced or recurrent endometrial cancer and is the first ADC to have randomized Phase 3 data in this setting.

Endometrial cancer is the sixth most common cancer in women and it's increasing in incidence. There's significant morbidity and mortality, particularly in late-line settings, and there is no standard of care in majority of patients whose cancer progresses despite the use of IO therapy like KEYTRUDA and chemotherapy.

This builds upon our expertise in the disease where we have two -- we have innovated with therapies, including with KEYTRUDA. And we're excited about these results. We will be talking to health authorities, and you'll see the data at an upcoming scientific presentation in the near future.

Sac-TMT is one of the eight antibody drug conjugates that we are excited about and having clinical development today. We have one of the largest and broadest ADC portfolios in late-stage development and covering important cancers. Our ADC pipeline brings a diversity of targets, bispecifics, and linker payloads. This provides potential opportunities to improve outcomes for patients and create unique combinations.

Now, I want to move on to another important part of our portfolio, which is MK-2010. In addition to building upon tissue targeting therapies such as sac-TMT, where over half of our studies are being done in combination with IO therapy with KEYTRUDA, we are also building out immuno-oncology with MK-2010, which is our PD-1 VEGF bispecific antibody.

We publicly presented data for the first time from a collaboration study that was initiated by LaNova, and this was presented at AACR this year.

The study demonstrated clinically meaningful data for MK-2010 as treatment for certain patients with advanced non-small cell lung cancer. For those in the first-line treatment-naive setting, the unconfirmed objective response rate was 55 percent among 11 previously untreated patients with PD-L1 positive non-small cell lung cancer at the 20-milligram per kilogram dose.

And what I like to look at is the waterfall. The majority of patients show tumor control or shrinkage. The safety profile of MK-2010 is consistent with what's observed with this new class of assets and allows us to be able to develop this drug potentially both as monotherapy, and importantly, in combination with other drugs in our portfolio.

We believe we are uniquely advantaged to fully explore the potential of the PD-1 VEGF access. While KEYTRUDA is central to our experience, much of what we have learned comes from combining it with different therapies and different mechanisms of action, including VEGF inhibitors. Although we are not sharing specific development plans today, as Dean noted, we are operating from a position of strength given the breadth of the studies we've conducted across multiple therapeutic classes.

In addition to the external knowledge about VEGF inhibitors and as emerging data comes about bispecifics, we have meaningful experience of our own. We have conducted multiple studies of KEYTRUDA combined with VEGF inhibitors, including Avastin combinations that have led to approvals beyond our own experience with a portfolio of novel agents that offer combination opportunities oriented towards combinations of the future rather than adding on to today's current standard, including ADCs like sac-TMT.

Together, our experience plus our portfolio provides a strong foundation as we plan MK-2010 development across multiple tumor types in a rapidly evolving oncology landscape.

So now let me turn to our innovative hematology portfolio. You have seen our recent announcement about the acquisition of Terns Pharmaceuticals, which brings us TERN-701. This asset further expands the portfolio in hematology despite multiple approved tyrosine kinase inhibitor, significant unmet need remains for improved efficacy, safety, and convenience for certain patients with CML.

The team at Terns did a fantastic job of developing a highly selective, potent oral allosteric BCR-ABL tyrosine kinase inhibitor designed to improve upon prior generation TKIs. It's high target selectivity potentially enables higher dosing while limiting side effects supporting improved therapeutic index.

In a Phase 1 study, TERN-701 demonstrated major molecular responses that are approximately 2 times and deep molecular responses that are approximately 2 to 3 times of those approved -- those compared to approved TKIs and historical data sets. We are very excited about this asset and look forward to advancing it into late phase development.

With TERN-701, our hematologic oncology portfolio now includes five assets that may be used across a variety of different hematologic malignancies in keeping with what our strategy is for Merck Oncology.

Nemtabrutinib is a potent noncovalent BTK inhibitor designed not only to bind reversibly to BTK, but it also had activity against other kinases and is designed to help prevent some of the common resistance mutations that occur with covalent BTK inhibitors.

Bomedemstat is an LSD1 inhibitor. This is a mechanistically exciting drug with potentially disease-modifying effects in chronic diseases like essential thrombocythemia and polycythemia vera.

Zilovertamab vedotin is a ROR-1 ADC currently ongoing in Phase 3 trials in diffuse large B-cell lymphoma, including a head-to-head study against Polivy. We have seen activity in GCB and non-GCB tumor cells and diffuse large B-cell lymphoma. We also have seen activity of ZV both as monotherapy and combination, and we are excited about the progress of this program.

MK-1045 is a CD19 T-cell engager potential utility not only in ALL, but across other hematologic malignancies. And then TERN-701 rounds out our portfolio.

So again, thinking back to our strategy, the same principles apply here. We have created and curated a hematology pipeline of drugs that have great potential as a single agent and combination.

And then finally, let me provide you a forward look at the readouts you can expect from our innovative pipeline. We're excited about the portfolio. We have assets with compelling activity that have led to approximately 60 Phase 3 studies in our late-stage portfolio.

That excitement and commitment to patients is leading to a series of readouts you've already started to see starting with TroFuse-005 in endometrial cancer. And we have a PDUFA date in October for I-DXd, an extensive-stage small cell lung cancer. There is a steady cadence of readouts extending through '27, '28, '29 across 10 new assets, reflecting the diversity of the portfolio and the broad reach we have.

I will now turn it over to Jannie to talk about the commercial opportunity.

Jannie Oosthuizen - *Merck & Co., Inc. - Executive Vice President and President, Oncology and MSD International*

Thank you, Marjorie. It's a pleasure to be here. I have the privilege of addressing you in my new role as President of our Oncology business unit and Human Health International Markets at a time of significant progress across our oncology portfolio.

Our dedicated teams have established a leading franchise around the world. We continue to execute with excellence across multiple tumor types, driving patient impact and access to our important cancer therapies in over 100 markets.

We have reached more than 4 million patients worldwide with our oncology medicines. Our suite of oncology products is approved in 58 indications across 25 tumor types, including two tumor-agnostic indications. This portfolio provides a strong foundation for the broad range of opportunities Dean and Marjorie outlined.

Our research colleagues continue to deliver compelling clinical advances, and we are excited by the reach and competitive pipeline. Importantly, the commercial organization, both in the U.S. and globally, is in place to deliver on that opportunity and further improve outcomes for patients.

Today, I'll focus on the near-term programs we're advancing with the same discipline and urgency that help establish Merck as a leading oncology Company. I'll close with our long-term commercial aspirations for our broad and diverse late-stage pipeline.

We remain confident in the outlook for KEYTRUDA, supported by continued momentum in earlier stage indications and ongoing strength in metastatic settings. Sales from early-stage indications represented more than 25 percent of total revenue in 2025 and are expected to increase further. Indications approved in the last year, including in certain head and neck, ovarian, and muscle-invasive bladder cancers will drive a large portion of growth.

And there remains potential opportunity for additional new indications both in earlier stage and metastatic disease. We have built a strong presence in GU and women's cancers, underpinned by the robust data KEYTRUDA continues to generate. By 2028, we anticipate that roughly half of KEYTRUDA's revenue will come from women's cancers and GU, reflecting the breadth of our clinical program spanning TNBC, multiple gynecologic cancers, RCC, and bladder cancer.

Our commitment to innovation and addressing the unique needs of patients and healthcare systems extends to KEYTRUDA QLEX, our subcutaneous pembrolizumab with berahyaluronidase alfa. The launch is off to a strong start. In the U.S., we have seen a good acceleration in adoption since the establishment of the permanent J code on April 1.

The adoption rate exiting the first quarter was in the mid-single digits, supporting our confidence that we are on track to achieve 30 percent to 40 percent peak adoption by the end of 2027. As expected, the majority of adoption is in patients who are on monotherapy regimens or combinations with other oral therapies.

A recent U.S. label update includes data evaluating patients' preferences between subcutaneous administration of KEYTRUDA and IV KEYTRUDA. Results showed 65 percent of patients preferred KEYTRUDA QLEX over KEYTRUDA IV where the most common reason being less time spent in the clinic.

Outside of the United States, we have received approvals in the EU and U.K. and some other markets. We have made good progress in certain markets and expect launches in additional markets later this year. We anticipate 30 percent to 40 percent peak adoption on average globally, with peak penetration varying by market.

We continue to be pleased with the impact we are having on certain patients with RCC and other VHL-associated tumors with WELIREG. We look forward to launching two additional indications for WELIREG later this year.

The first one is LITESPARK-022, the combination of WELIREG with KEYTRUDA in adjuvant RCC, and it has a PDUFA date of June 19 this year. This builds on the foundation set by KEYTRUDA monotherapy based on the KEYNOTE-564 study, and if approved, would be the potential first IO combination treatment option in the adjuvant RCC setting. The study demonstrated meaningful improvement in disease-free survival.

The second one is LITESPARK-011, the combination of WELIREG with Lenvima in certain previously treated advanced RCC, and it has a PDUFA date of October 4 this year. This is the potential first and only HIF-2 alpha inhibitor plus a VEGF TKI regimen for patients whose disease progressed following anti-PD-1, PD-L1 therapy, and a demonstrated superior PFS versus a modern TKI with improved duration of response. With these new opportunities in RCC as well as the future potential in combination with zanzalintinib, we believe WELIREG has multibillion-dollar peak commercial potential.

Next is I-DXd, our B7-H3-directed ADC in collaboration with Daiichi Sankyo. I-DXd has the potential to address unmet need for patients starting in extensive-stage small cell lung cancer. Small cell lung cancer is a deadly, rapidly progressive cancer with high unmet need and very poor prognosis. Approximately 10 percent to 15 percent of all lung cancers are small cell, and about 70 percent of patients are diagnosed with extensive-stage disease. Unfortunately, the five-year survival rate remains just 4 percent for those with distant metastases.

The FDA has granted priority review for I-DXd in certain adults with previously treated extensive-stage small cell lung cancer and set a PDUFA date of October 10 this year. This marks an important step for this potential first-in-class therapy.

Beyond extensive-stage small cell lung cancer, we have ongoing registrational trials in second-line esophageal squamous cell carcinoma and metastatic castration-resistant prostate cancer, which represents a much larger patient opportunity. We're also exploring the combination of I-DXd with gocatamig, our T cell engager, also in collaboration with Daiichi Sankyo in small cell lung cancer.

As Marjorie described, our development program for sac-TMT is extensive and primarily focused on populations where we aim to be first-in-class. We are also exploring opportunities where we will be competitively advantaged due to the differentiated clinical profile of sac-TMT.

Here, we outline the patient opportunity for each -- for each potential indication. The breadth of this program underscores why we believe sac-TMT has the potential to be a cornerstone ADC across a variety of different cancers.

sac-TMT is being evaluated in the broadest range of disease and treatment settings of any TROP-2-directed ADC with studies across early to late-stage disease in more than seven tumor types, representing up to approximately 200,000 patients in the U.S., E.U., and Japan.

Building on Marjorie's comments, I want to emphasize the significance of the TroFuse-005 results. Patients with metastatic endometrial cancer have a medium overall survival of less than one year after progression on platinum chemotherapy, and there is no standard of care for the majority of patients whose disease progresses following IO and chemotherapy.

sac-TMT is the first and only TROP2 ADC to demonstrate an overall survival benefit in endometrial cancer compared to chemotherapy in these patients with advanced or recurrent endometrial cancer. An approval would further build on our deep expertise in gynecologic cancers. We already have multiple indications and reinforce sac-TMT's role as a potential transformational therapy in this space.

We are building from a strong foundation as we advance the next wave of oncology innovation. We continue to see greater than $25 billion in nonrisk-adjusted commercial opportunity from our oncology late-stage pipeline alone by the mid-2030s. Importantly, this does not include the recent acquisition of Terns Pharmaceuticals, which has multibillion-dollar peak commercial potential on its own.

Over the coming years, we have the opportunity to bring 14 new products to market for the treatment of cancer across more than 80 new indications. As our product mix diversifies, we expect to establish a meaningful presence in hematology, building on our leadership position today in solid tumors.

In summary, we are highly confident in our oncology position and believe our strong presence will extend well into the next decade.

With that, I'll turn it over to Dean for closing remarks.

Dean Y. Li, M.D., Ph.D. - *Merck & Co., Inc. - Executive Vice President and President, Merck Research Laboratories*

So thank you so much for your attention here. This evening, we spoke to how we have executed on our oncology strategy, building on our strong foundation with KEYTRUDA while advancing an increasingly diversified pipeline of oncology candidates.

In total, as you've heard, we have approximately 60 ongoing Phase 3 trials at this moment. I would imagine more will be opened. The broad impact of KEYTRUDA right to roadmap for the future as we develop molecules spanning three pillars of biology, immuno-oncology, precision targeting as well as tissue targeting, especially with ADCs.

Now we're deploying these candidates with the goal of maximizing benefit risk and convenience to patients while providing exceptional value for payers. Hopefully, today's presentation has contextualized our strategy and how we prosecute clinical trials. We believe that we are in a strong position to further improve patient outcomes in oncology.

I just want to emphasize that we're here at ASCO, and we're focusing on diversifying in oncology. But we've also said in 2021 that not only do we need to diversify oncology, we have expanded in other therapeutic areas. And I just would emphasize the cadence of readouts that you've just shown, especially what Jannie showed in the last is happening in the other therapeutic areas as well, in cardiometabolic with WINREVAIR, OHTUVAYRE, and the potential approval of enlicitide and the follow-on compounds that follow that in immunology with tulisokibart as well as other immunology assets moving forward, especially in ophthalmology, where we have two assets moving fast.

And in HIV, we've increasingly shown islatravir as a backbone. So I think this concept of us diversifying and expanding our pipeline since 2021 is important and relevant, not just for oncology, but also across other therapeutic areas and spanning multiple modalities, including small molecules and vaccines, macrocyclic peptide, and complex and conjugated biologics.

And with that, I will turn it over to Peter for questions and answers.

QUESTIONS AND ANSWERS

Peter Dannenbaum - *Merck & Co., Inc. - Senior Vice President, Investor Relations*

All right. Very happy to take your questions. If you could state your name and your firm when asking your question, that would be helpful.

So maybe Chris Schott to start.

Christopher Schott - *JPMorgan Chase & Co - Analyst*

Just maybe a two-parter on VEGF PD-1. Maybe just first, if you can just provide some context of your view on the data we saw at this conference and how that informs your approach as you consider development programs for 2110?

And then just when we think about that development program, do you think we've had enough derisking of the mechanism where we should think about Merck running a broad set of studies in a wide range of indications similar to what you do with TROP-2? Or is this an approach where we could think about maybe a more gradual approach?

I know you're not disclosing it, but how to think about that.

Dean Y. Li, M.D., Ph.D. - *Merck & Co., Inc. - Executive Vice President and President, Merck Research Laboratories*

Oh, so clinical development. Speak to that, Marjorie.

Marjorie Green - *Merck & Co., Inc. - Senior Vice President, Head of Oncology, Global Clinical Development*

Thanks so much for the question. I think we are all eagerly awaiting the data presentation of the HARMONi-6 data. And I want to congratulate the investigators and Akeso for running a well-conducted study. With this, the impact it has is that -- I think it's increased excitement, but also has left a lot of questions still remaining. And that's what I think your question is getting at.

So what was impactful to see was that I think that the hazard ratio for PFS have been 0.6. And unlike the other VEGF checkpoint inhibitor historic studies of chemotherapy combining with IO VEGF, the hazard ratio here was very close to the PFS hazard ratio. And this would actually include HARMONi-2, which had both squamous and nonsquamous in there, that hazard ratio that had a much larger drop than you saw here.

The other thing that stands out is the AE profile was what was expected generally for adding in another mechanism, chemotherapy plus a checkpoint inhibitor, now will have a little bit more toxicity than the chemotherapy alone or a checkpoint inhibitor alone. And then you're adding a VEGF inhibitor on top of that, albeit the therapeutic index for safety does appear to have improved a bit with this particular kind of structure and formatting.

So the AE profile is what's expected. It was tolerable, had low rates of discontinuations and no surprising adverse events were noted. They were very careful in how they talked about patient selection for this because of the historical challenges Avastin had in this space. So particularly in talking about cavitation, about blood vessel involvement.

There also was an age cap of over 75. And we know that this is not a disease squamous cell -- non-small cell lung cancer is not a disease of young people. It's a disease of people who have been smoking heavily in their life and often older. I think in the United States, the median age for this might be around 70.

So there -- and when you look at the hazard ratios for both PFS and for OS, they are not comparable by age. So I think it's clinically compelling, the curves. They overlap, then they separate. Open questions. Does this translate into an older population? What is the reason that you have differences in outcomes and robust sample sizes for those younger than 65 and those older.

Is there an AE profile? What's going on there? Is this sort of a random chance? It's not known. And the median follow-up is before that really -- you don't know what the OS is going to end up being because of the amount of censoring. It's still fairly early. So are those curves going to stay apart? Or are they going to start to come back together with time? And that's always been this open question when you look historically at the majority of studies that have been conducted with VEGF inhibitors and checkpoint inhibitors in non-small cell lung cancer.

So I dissected it, and the question is sort of what does that mean? And I think what it shows is that there are likely situations where the PFS will translate into a clinically meaningful overall survival. I would like to see this replicated in a global study. The Chinese investigators do an amazing job of running really clean studies. And so I want to see this in a global study and what the data will look like.

The other open questions, you still have heterogeneity results and other tumor types. As far as the -- even in non-small cell lung cancer, if you think about the different HARMONi studies and the shapes of the curves and the hazard ratios, they're not as consistent as this.

So to me, that means that there's still open questions about, is this something that will truly unlock benefit? Everywhere, you have seen a VEGF inhibitor work and a checkpoint inhibitor work. And I think the answer is still we don't know. But this is a positive finding, I think, it's great for patients in China, as I discussed and said.

And for us, we've always in all of our studies and everything we do, including our sac-TMT program, we have a disciplined and very data-driven development program. And so we use all of those studies that you saw us flash up looking at all of our knowledge about VEGF inhibitors and checkpoint inhibitor KEYTRUDA combinations.

We look at the emerging data. And then we're also thinking about the future because we're very excited, for example, about the OptiTROP-Lung05 data. We're excited about our KRAS G12C program. We're thinking about what therapy is going to be looking like in a couple of years, not what it looks like today as we're developing our plan. We have a Phase 3-ready asset with MK-2010.

Peter Dannenbaum - *Merck & Co., Inc. - Senior Vice President, Investor Relations*

Daina?

Daina Graybosch - *Leerink Partners LLC - Analyst*

Daina Graybosch from Leerink Partners. In Kelun's OptiTROP-Lung05, I thought sac-TMT plus pembro looked pretty competitive when you compared it indirectly the pembro plus platinum-based chemo, both in 407 and 189. And I wonder what's holding Merck back from starting a head-to-head study with sac-TMT versus 189 and 407 beyond maintenance for 407?

Dean Y. Li, M.D., Ph.D. - *Merck & Co., Inc. - Executive Vice President and President, Merck Research Laboratories*

So I'm going to turn this to Marjorie, but I will comment about many of my interactions with many of you over the last two to three years. And I would just sit there, and I just would remind that when we first moved in sac-TMT, I think many questions were asked of why are you coming in to TROP2 ADC when there's two ahead of you?

And I think what we said there is we don't think all the TROP2 ADCs are the same, just like we don't think all the HER2 ADCs are the same. I think the other sort of thing that were remarked to us is that we thought that if you could get it right, you could be first in lots of tumors outside of breast and lung. And I think the endometrial data suggests that that may be possible.

Now the question is because people said, well, you guys blew this out in 17. I've actually gotten questions of why did you blow it out so much? And now I understand your question is: Why aren't you blowing it out further? Is that what I understand?

So with that, I'll turn it over to Marjorie.

Marjorie Green - *Merck & Co., Inc. - Senior Vice President, Head of Oncology, Global Clinical Development*

Yes. No, thanks for the question. And I said our strategy, we are always looking to where we think cancer therapy is going to be. And so thinking back to when we started our program, we recognized from data in 407 and 189 from emerging therapies, and just biologically, we know that lung cancer is not one disease.

And there is going to be increasing fragmentation of non-small cell lung cancer, including those who are eligible for KEYNOTE-189. And so we tried to think about where could we add the greatest value, considering that those who have non-squamous cell lung cancer have -- often have the RAS mutations, and that's going to be more subdivided into different therapies.

There was the biggest opportunity for those who had squamous carcinoma and needed something to help give them long, durable remission. That's what's led to that program.

The other one, TroFuse-007 was based upon -- there are people who don't want to give chemotherapy necessarily to everyone because they're not certain it's going to add benefit and high expresser PD-L1 scores. And so we wanted to show that, yes, we could do that. And again, further help to characterize different opportunities for clinicians and patients of how you could use this drug.

We didn't have the OptiTROP-Lung05 data when we were designing our program. And so we get -- had to think about how is the clinical practice going to change and recognizing where peer companies were, how do you want to develop?

The other thing to consider is that there can be approaches where you combine ADCs and chemotherapy together. So if you're going to do a 189 head-to-head and try and take these populations together and to sort of replace, it is that you want to ensure that you've got really robust efficacy and some people have taken, let's combine chemotherapy in the ADC together.

And there is one potential replacement study that's out there. But the combinations of therapy, when you look at other ADC chemotherapy combinations and some of the ones done in lung cancer, the response rates have not increased, suggesting the benefit may actually be the maintenance approach. So are you going to get more toxicity? Are you going to impact the doses of either the ADC or the chemotherapy by combining them together and then adding a checkpoint inhibitor?

And so I think our maintenance approach is where we think the biggest benefit is going to be there from what we knew when we started that study. I don't speak to the future too much because it's a highly competitive environment, as Angus who's in the room talked about in his [Fierce Pharma] article. But I do think that it is important for us to look at our portfolio and look at our OptiTROP data and think about -- it's very consistent across every subgroup. It's consistent across histologies and there's still opportunity there. And we have lots of things we can combine with in our portfolio.

Peter Dannenbaum - *Merck & Co., Inc. - Senior Vice President, Investor Relations*

Great. Thank. Steve Scala?

Steve Scala - *Cowen and Company LLC - Analyst*

Many thanks. Steve Scala from TD Cowan, two questions. It would seem the OptiTROP-Lung06 trial is a very important trial that's able to answer some of the control arm questions, including the one just asked, but it wasn't on any of your slides.

Can you speak to the trial and your level of confidence that this could be a successful trial? I understand it reads out later this year.

And secondly, sac-TMT China-only Phase 2 data in second-line endometrial, is that representative of what you observed in the Phase 3 TroFuse-005, or will the magnitude differ between the trials, magnitude of benefit? Thank you.

Dean Y. Li, M.D., Ph.D. - *Merck & Co., Inc. - Executive Vice President and President, Merck Research Laboratories*

I'd give it to you. But I would just say that in relationship to the Phase 3, I think one of the things is that will be presented at the appropriate time as we move forward with regulatory agencies, but –

Marjorie Green - *Merck & Co., Inc. - Senior Vice President, Head of Oncology, Global Clinical Development*

Yeah, no, thank you. So the OptiTROP-Lung06 study, and I am having a senior moment right now, and I'm way too young to have a senior moment. I think this is the one in the very low PD-L1 expressor, as I've seen -- not -- if you all know this better than I do, which is really a shame, that Kelun is running right now.

I can't forecast and speculate what the results are going to be about it. We've seen very consistent data from Kelun in non-small cell lung cancer. You've seen it in EGFR mutated non-small cell lung cancer. You've seen it in 05. You've seen efficacy results of the combination of pembrolizumab and sac-TMT that are very compelling at high efficacy.

And you've seen it across a range of PD-L1 expression levels, and particularly that hazard ratio. PFS for those who had low PD-L1 expression level in their tumors was quite robust. So I am as optimistic as I can be about a Phase 3 study that is ongoing and is due for readout.

The question I think that you're asking about endometrial cancer is how predictive is the data generated in China to what we get in the global study. And I think one of the things I'll say is someone who's worked on antibody drug conjugates in three different companies is they are fairly consistent when you look at response rate, duration response, and that translates into overall survival often.

And so I can't forecast, as Dean said, what the TroFuse-005 study looks like. You'll have to wait until we're presenting it publicly, but it's compelling data that we think that we were able to have confidence in from the Phase 2 data enough to start the Phase 3.

Peter Dannenbaum - *Merck & Co., Inc. - Senior Vice President, Investor Relations*

Great. Thanks, Steve. Michael Yee?

Michael Yee - *UBS AG - Analyst*

Michael Yee from UBS. With sac-TMT, it would seem to me that, obviously, you have the potential to also combine with a PD-1 VEGF. To what extent are you generating data either with 2010 that you are observing? Or that your partner Kelun in China is also generating data with sac-TMT with other novel agents including other PD-1 VEGFs that could be generating data that you could be learning from?

Dean Y. Li, M.D., Ph.D. - *Merck & Co., Inc. - Executive Vice President and President, Merck Research Laboratories*

Yes, it actually gets a little bit to -- I think it was Courtney's question, is when you ask us what future looks like, one of the things that we ask ourselves is what will the future look like for a PD-1 in relationship to sac-TMT? And so that's something that, clearly, has been on our minds and clearly on the minds of our partner, Kelun, as well.

But with that, I'll just ask Marjorie. Any comments you wanted to make?

Marjorie Green - *Merck & Co., Inc. - Senior Vice President, Head of Oncology, Global Clinical Development*

I think that we have not publicly talked about our plans of sac-TMT in 2010. And so I'm going to keep that to myself at this moment. The same thing, Kelun's got their own stuff that they're doing as well. And so there's no public information available this time. Stay tuned.

Peter Dannenbaum - *Merck & Co., Inc. - Senior Vice President, Investor Relations*

Great. Thanks, Michael. Maybe in the back. Trung?

Trung Huynh - *RBC - Equity Analyst*

Trung Huynh from RBC. So some of your VEGF PD-1 competitors, they're optimistic for PFS-based approvals in first-line lung cancer. If you have a look at all of your TroFuse lung studies, they use OS as the primary endpoint. Is there a mechanistic nuance here? Does the FDA view ADCs differently than IO bispecifics for approval just based on PFS?

And then does HARMONi-6 make you want to move faster? Slower? Or does it not change your Phase 3 development timelines for this class? I know you mentioned you're not going to share your development timelines, but could we be sat here next year knowing what that Phase 3 program is? Your peers are accelerating quickly.

Dean Y. Li, M.D., Ph.D. - *Merck & Co., Inc. - Executive Vice President and President, Merck Research Laboratories*

I love how the questions come. What I'll first say about the FDA is the FDA in the fields have been reasonably consistent. OS is a really important endpoint. And I would just emphasize, it's not just important for the FDA and regulatory agencies.

The payer who's being asked to pay for antibody-drug conjugates over chemo, they have some say in this. And so we think it's very important to keep that in mind, but I don't know how you want to dance around the rest of his question.

Marjorie Green - *Merck & Co., Inc. - Senior Vice President, Head of Oncology, Global Clinical Development*

Well, I think the question -- PFS is a clinically meaningful endpoint across multiple diseases. It really is. And lung cancer, unfortunately, has been a disease where there have not been many really remarkable advances until maybe the last 10 to 15 years. And so people have wanted to see overall survival improvement.

As outcomes get better and better, it becomes more difficult to actually demonstrate overall survival. And so there may be a future where PFS could be considered in the United States as the only endpoint needed as long as you can show lack of detriment. You're not hurting people with the OS and that people are getting some benefit there.

I don't know that we're there today. And if you think about antibody drug conjugates, they are much more potent cytotoxics that are given directly to the cancer cells than IV chemotherapy, and you would expect a profound PFS benefit that, hopefully, would translate into overall survival.

And so I think that there our differences and studies and endpoint somewhat based upon the timing and the initiation of the studies rather than a fundamental belief in the mechanistic action of different drugs.

And as to your second question of how excited I am or the speed at which I'm going there, we are -- we have a Phase 3-ready asset. We are data-driven. We are disciplined. We have a great portfolio that can be combined with, and you'll have to stay tuned.

Peter Dannenbaum - *Merck & Co., Inc. - Senior Vice President, Investor Relations*

Carter?

Carter Gould - *Cantor Fitzgerald LP - Analyst*

Carter Gould, Cantor Fitzgerald. Dr. Green, you alluded to your biomarker strategy for, I believe, for your TROP-2. Can you provide any further detail there and how you're thinking about deploying that? There's additional work that needs to be done before we see that rolled out. And any details particularly around differentiating versus some of your competitor approaches with their -- there were biomarker strategies in the space?

Dean Y. Li, M.D., Ph.D. - *Merck & Co., Inc. - Executive Vice President and President, Merck Research Laboratories*

Yes. So I'll just say something and I'll hand it to Marjorie. I think it's important that we have -- that one has a biomarker plan and a biomarker ability, but that biomarker ability can be broadly distributed, especially in the United States and Europe and other places.

But the other sort of thing I just want to emphasize what Marjorie said is that just because you have a biomarker, it doesn't mean that you're going to use that biomarker in every indication.

But with that, Marjorie?

Marjorie Green - *Merck & Co., Inc. - Senior Vice President, Head of Oncology, Global Clinical Development*

Yes. No, no. Thank you. We haven't been as public about our biomarker plan as some peer companies have been in talking about what they're doing. And we have extensive IHC capabilities that through the very large development program that we've done with our partners in China, you also might have seen some of the digital pathology information that has come out at ASCO this year that we are working on.

And so as Dean said, it is not a one-size-fits-all approach. And I think it underlies the mechanism of antibody direct conjugates and how you're trying to predict response because there are multiple pieces that go in. And each Company's drug is different, the ADCs are different and how you might approach selections difference as the antibody against the target, how well does it internalize, what does the linker payload do?

What is the expression level on different tumor cells? How effective is the bystander effect? How much efflux pump is there in a particular tumor type? All of those can change response and therefore, prediction of response may vary tremendously based upon the ADC.

So I can say is that, that probably gives you -- I can't tell you because the drugs are different. The biomarkers are different. The tumors are different. The settings are different. And so it depends but we are well set up in our ongoing Phase 3 studies.

Peter Dannenbaum - *Merck & Co., Inc. - Senior Vice President, Investor Relations*

Courtney?

Courtney Breen - *Sanford C Bernstein & Co LLC - Equity Analyst*

Courtney Breen. Just a question on the heme portfolio that you characterized on the slides today. This hasn't necessarily been an area that Merck has been in commercial markets with in the past. And certainly, you've done some deals recently that perhaps others had stepped away from.

And so I would love to understand kind of why is now the right time for Merck to succeed in this space? And why are these assets going to set you up for success here, particularly given kind of some others have accelerated past you, thinking about Lilly with pirtobrutinib and some of the others as well?

So I would love to just hear a little bit about why you believe now is the right time for Merck?

Dean Y. Li, M.D., Ph.D. - *Merck & Co., Inc. - Executive Vice President and President, Merck Research Laboratories*

I'll let her -- Marjorie touch on the different assets, especially the ones that you mentioned. And then I'll make some comments in relationship to our ambition to move into heme, especially after -- we felt that it was a really important place for us to make a good foray in because it's such an important part of oncology.

Marjorie Green - *Merck & Co., Inc. - Senior Vice President, Head of Oncology, Global Clinical Development*

Yes. No, thanks for the question. Each of the assets, we think, is compelling and has the ability to make a meaningful benefit for people with different hematologic diseases. And many of these diseases are ones that are often chronic in nature. And so thinking about different assets such as like nemtabrutinib; this is a drug because it has a slightly broader kinase activity and it also has a bit of a flexible binding that can adapt to different mutations.

Preclinical studies have demonstrated that there are low rates of development of resistance in the target over time when compared to other laboratory animal model studies of other assets and what's been published, for example, in BRUIN.

And so it's that kind of what can you get from that is potentially people do not develop resistance. And with the mutations of the binding site, that then allows for treatment across multiple lines or the preserved ability to continue to use a drug like nemtabrutinib. And so that was what was really interesting to us about it.

I think that our studies also were done to truly because this is a disease where people have been using sometimes the same therapy since the first-generation drugs for a long, long time, and they haven't moved off of them, to really make sure that we are comparing against what is a first-line standard of care. We didn't combine multiple populations into a study and try to sort of say this works.

So we really took a very different development approach to reflect the practice of physicians and the needs of the patient. So that's why we're excited about nemta and why we've developed there.

Very similar considerations have gone into the other assets. So I talked about ZV, zilovertamab vedotin. And Polivy is a similar drug, different target that's already approved. But we saw that in some of their initial Phase 3 data sets that the majority of benefit was in one subpopulation of diffuse large B-cell lymphoma, whereas ZV works in both.

So those are the kind of approaches that have led to our development and why we continue to be excited about the portfolio.

Dean Y. Li, M.D., Ph.D. - *Merck & Co., Inc. - Executive Vice President and President, Merck Research Laboratories*

I do want to pick up on one of the things that you asked, which was from a commercial standpoint. And I think it's appropriate that Jannie make a comment because Jannie's experience and solid tumor in this, we are making a foray in heme both, quote-unquote, benign heme and heme malignancy.

And I think I should turn it over to Jannie.

Jannie Oosthuizen - *Merck & Co., Inc. - Executive Vice President and President, Oncology and MSD International*

Yes, thank you, Dean. And I would just say, we've always had an ambition to diversify beyond KEYTRUDA, right? And we're doing that in solid tumors. We've always -- and Sophie can speak to this as well, it's been an ambition to also diversify into heme malignancies.

We know it is different to solid tumors, but it is adjacent. We believe that we have significant capability that we can scale across hematology as well. And again, I think even though we had the ambition, we move with the science, we move with products that we think is going to bring meaningful value.

And I think we now have five assets enhance that in and that can take us down that path. So I don't know if there's something that you would add.

Sophie Opdyke - *Merck & Co., Inc. - Senior Vice President, Global Oncology Marketing*

I think to your point, we have now critical mass in terms of hematology to be able to build the commercial organization. We are looking at a disease over a large value pool like CLL over DLBCL, but also in an area where there has been no innovation like essential thrombocythemia and we believe that we can kind of shape the market with new and effective therapy.

Dean Y. Li, M.D., Ph.D. - *Merck & Co., Inc. - Executive Vice President and President, Merck Research Laboratories*

But also in relationship to your question, I would just emphasize, when we're talking about -- we're trying to give you a sense of the cadence of data readouts. I mean, I think we have listed three PCD dates in 2027 for heme assets and then an additional one in '29.

So we're trying to lay out -- these are coming and you'll see it, and it's coming sooner than I think many people recognize.

Peter Dannenbaum - *Merck & Co., Inc. - Senior Vice President, Investor Relations*

Great. Jason?

Jason Gerberry - *Bofa Merrill Lynch Asset Holdings Inc - Analyst*

Jason Gerberry, Bank of America. So I just have a question on OptiTROP-Lung05, and I preface by saying feedback we hear from a lot of oncology KOLs is reluctance to subject patients to maybe ADC toxicities in the PDL high segment.

So I'm just curious if you can speak to in OptiTROP-Lung05, any color on the management of the AEs through support of care, be it either anemia requiring transfusions or any prophylactic measures with stomatitis? And then if those measures are implemented in the counterpart TROP-2 study?

Marjorie Green - *Merck & Co., Inc. - Senior Vice President, Head of Oncology, Global Clinical Development*

Yes. Thanks for the question. Benefit and risk are always critical for the patient and the oncologist, and we agree with that. And the reason you would want to consider something beyond KEYTRUDA in this population is that while survival is good, there's still a lot of people who, unfortunately, have progression and die with high PD-L1 expression tumors.

So antibody drug conjugates are still cytotoxic therapy in the current generation that are out there. And so they will have cytotoxic activity or side effects. And most of them are related to where there's expression of TROP2, so you get GI toxicities with them or it's related to some small circulation of the payload, and that's where you're getting some of the hematologic toxicities.

These are toxicities that physicians are very, very comfortable in managing. In the OptiTROP-Lung05 study, the AE rate reporting, so the way AEs are reported in China studies, is that all hematologic labs are reported as adverse events, whether a physician thinks they're clinically meaningful or not. That doesn't happen necessarily in global studies.

There was not use of primary growth factor support in this study. For mouth sores for stomatitis in China, they do not routinely use steroid mouthwash. They'll use baking soda mouth rinse, oral hygiene, other kind of care events. And in our global studies, we are very aggressive with secondary use of growth factors as well as mouth care, including oral stomatitis management because the study was started a while ago, and we've learned and have really adapted.

I think there is a question that people sometimes ask about, will AEs in a China study be the same as you would see in a global study? And you can look at there are other TROP2 ADCs, who have very similar rates of stomatitis and as well as low grade and most of them are thankfully low grade as well as Grade 3, and they're fairly consistent across most of the studies.

So it's going to be -- does this affect quality of life? Are people going to be able to take it? And I think with these kinds of adverse effects, particularly low-grade ones that, yes, hematologic ones tend to not be disruptive for the patients. And it's that benefit is the PFS and OS there for these patients, and that's what will change instead of just using KEYTRUDA as a monotherapy.

Peter Dannenbaum - *Merck & Co., Inc. - Senior Vice President, Investor Relations*

Jon Miller?

Jonathan Miller - *Evercore Inc - Analyst*

Jon Miller from Evercore ISI. I'll ask a question about something else big at this conference that we haven't talked a lot about, and that's the RAS space.

Dr. Green, you mentioned -- do you expect to see, for instance, lung get more and more fragmented? You specifically called out RAS is a potential population where that's going to happen. But when I look at your pipeline, I see a relatively thin list of assets in that space compared to a large list of assets in development across the field.

So what are your plans for RAS? How do you think that is going to develop in lung and beyond? And when can we hear more from you about the ways moving forward?

Dean Y. Li, M.D., Ph.D. - *Merck & Co., Inc. - Executive Vice President and President, Merck Research Laboratories*

I'm going to take a first shot and then give it to Marjorie, but I just would just -- when one thinks about the RAS space, it may be reasonable. RAS is in so many tumors. But a simple way to think about is think about lung, pancreas, and CRC.

The first movers in RAS were really important in G12C. I think that some of you have asked, why are you doing a RAS program? And the concern that we had back in 2018, 2019, was whether those RAS molecules could really survive the ability to get into first-line lung. And this goes to one of the comments that Marjorie says, combinability is critical. So the quality of your molecule and the combinability, in that case with a PD-1, is critically important.

So we have a study that Marjorie will talk about, which is we're hoping to lay that down in first-line lung for G12C, which will be important. We also look at the G12C and ask ourselves, what does it teach us about other tumors? G12C is not prevalent in pancreas, but it is, in some sense, in CRC.

So the ability to see, even in a small percentage, what that monotherapy looks like and how well it combines with the other medicine that's not PD-1 in that standpoint, it's cetuximab. And so that data is coming out.

We believe that we have to be outside of G12C clearly, and we have an asset 4716 that is advancing with pace. The way I would simply say it, it's a non-G12C broader RAS molecule. We haven't declared what it is exactly, but that's moving at pace in clinical development as well.

But I think it would be worthwhile to give an update of how you look at that data, especially the ones that we hope to advance, especially in G12C and first line in lung and in CRC.

Marjorie Green - *Merck & Co., Inc. - Senior Vice President, Head of Oncology, Global Clinical Development*

Yes. No, thank you so much. I think Dean really highlighted what -- how we've been thinking about this, and it does fit in with our strategy is that to have the best effect, you need to be able to combine and calderasib, and you saw the breakthrough therapy designation. I talked about it.

It has really well-tolerated AE profile combined with pembrolizumab. And the activity is compelling. And so we have a series of Phase 3 studies in non-small cell lung cancer. We have one in those who have TPS scores greater than 50 percent, KANDLELIT-004.

And then we also have one with QLEX combined with KEYTRUDA QLEX where we are going head-to-head against the 189 regimen, because we are so impressed with the tolerability combinability, the importance of hitting a driver mutation with a very potent and clean targeted therapy.

We also have studies in the adjuvant setting and in unresectable non-small cell lung cancer. And then because this is combinable and you might have seen the data in colorectal cancer, we have pretty robust monotherapy activity with our G12C inhibitor compared to some of the peer assets that have published information. And when we combine with cetuximab and chemotherapy, the responses are quite robust and durable. So we have a study ongoing in colorectal cancer.

So we have a broad development program there. And as Dean said, we have MK-4716, but we're not talking about it yet. So this is an important pathway. We want to make certain that we've got assets that meet those characteristics of being single agent active and combinable to ensure that we are improving therapeutic index and ability to benefit patients.

Peter Dannenbaum - *Merck & Co., Inc. - Senior Vice President, Investor Relations*

Mohit?

Mohit Bansal - *Wells Fargo Securities LLC - Analyst*

Mohit Bansal from Wells Fargo. Before I start, first of all, congratulations on the data. Since I congratulated, I can ask two-parter, probably.

So the question is, so since you talked about combined ability, I think how do you think about the combined ability of the TROP2 ADC and VEGF PD-1 here? And when you think about the combinations in the future, I mean, yes, you have a Phase 3-ready asset in VEGF PD1, but the competition is a few years ahead.

How would you think about partnering your sac-TMT with other PD-1 VEGF that are out there to get to the market sooner? Because with KEYTRUDA, you did the strategy, you played the strategy where it worked out really well for you. So I just want to understand that part.

Dean Y. Li, M.D., Ph.D. - *Merck & Co., Inc. - Executive Vice President and President, Merck Research Laboratories*

So if I understood, the question is: When you have a really important compound, are you willing to combine it with other people's compound? Almost agnostic, a little bit of what we did with KEYTRUDA in some sense. I would say that we're always open to that, and we're always open to that, not just in oncology, but we're open to that in non-oncology where you have really important assets, whether it's WINREVAIR or something like that.

So that's something we've always considered. And that's something that, depending on the opportunity. But having said it, I do think that -- as you specifically talked to PD-1 VEGF, we have a PD-1 VEGF that we're quite confident in, and we have a really good portfolio of ADCs and other compounds that you could combine.

And one of the things is when we think about those studies, one has to think about the speed, the rigor, and you have to balance off sharing it and owning 100 percent of that combination, but you always have to balance it.

But I think your point is well taken, and it's something we think about not just for our PD-1 VEGF, it's not just what we think about our sac-TMT, but it's with any asset that we have that we think could really have broad implications. So we are open to it and people know that we're open to it.

We did it for KEYTRUDA. We will do it for other compounds in our portfolio, and that answer is not just limited to oncology.

Peter Dannenbaum - *Merck & Co., Inc. - Senior Vice President, Investor Relations*

Malcolm?

Malcolm Hoffman - *Bank of Montreal - Equity Analyst*

Malcolm Hoffman here for Evan from BMO. TROP-2 agents have been more challenged in non-small cell lung cancer. So much of ASCO because this year, it feels like a discussion on how your TROP-2 can be both a leader in non-small cell and a better competitor for some emerging PD-1 VEGF agents.

Can you talk about, first, why you think we are seeing such efficacy in non-small cell despite other TROP-2 failures? And second, what you think we have learned from this ASCO about competitive positioning of sac-TMT versus these other PD-1 VEGF agents?

Dean Y. Li, M.D., Ph.D. - *Merck & Co., Inc. - Executive Vice President and President, Merck Research Laboratories*

So I'm going to make a flippant comment that got picked up by some of you, is that correct, at JPMorgan where I said, not all ADCs are the same. Some can be too loose, some can be too tight, and some can be just right.

And with that, I'll hand it over to Marjorie.

Marjorie Green - *Merck & Co., Inc. - Senior Vice President, Head of Oncology, Global Clinical Development*

So yes, I think when we first started working with this, I was talking to the team about Goldilocks and the three bears, and depending upon where you are raised, particularly if you're our China team, they didn't know that story. And so they looked at me very strangely.

They're not the same. I think that's the hard thing is we think that the ADCs are similar and they're truly not. And so I can't speculate about data sets that you've seen, but you've seen high response rates durability in nonrandomized data sets in the first-line setting with TROP2 ADCs.

And I think that there's a lot of different factors that go into successes of studies. But we're very confident in the data that you see, you can't do much better than a randomized Phase 3 well-conducted study, like we've seen with OptiTROP-Lung05 as well as the other data sets that they've generated.

So it's a non-answer, I think, but it goes back to Dean's part. They're not all the same.

Dean Y. Li, M.D., Ph.D. - *Merck & Co., Inc. - Executive Vice President and President, Merck Research Laboratories*

And I would just emphasize the linker payload of Kelun, this TROP2 ADC, as you can see from the slide, is not the only asset. Similarly, I would just say the linker payload of Daiichi Sankyo that they really pioneered is also important, and we don't just have one asset.

But how you position these different flavors given their molecular design differences, one has to think thoughtfully about those differences. But I don't -- I want to make sure we respect very much the linker payload of Kelun and go back to the slide.

It is not just one compound. And we respect very much the linker payload, which is different for Daiichi Sankyo. And you see how we advance them but we're not -- we're advancing them in different ways and different tumors.

Peter Dannenbaum - *Merck & Co., Inc. - Senior Vice President, Investor Relations*

All right. Maybe just a couple of more questions. Nick?

Nick Jennings - *Goldman Sachs - Analyst*

Nick Jennings, Goldman Sachs. A question on read-throughs or learnings from OptiTROP-Lung05. First, in lung. What, if anything, in the data makes you feel more confident in the maintenance setting or adjuvant setting?

And then outside of lung, are there any derisking things that you see for other indications that you're running in TroFuse?

And then finally, is there anything that you can share in terms of prospects for any other interim reads for the TroFuse trials? Are there any trials progressing where you could actually see an interim?

Dean Y. Li, M.D., Ph.D. - *Merck & Co., Inc. - Executive Vice President and President, Merck Research Laboratories*

So I'm going to turn it over to Marjorie. But as you guys know, famously, we do not comment on interim analysis.

With that, Marjorie.

Marjorie Green - *Merck & Co., Inc. - Senior Vice President, Head of Oncology, Global Clinical Development*

We don't comment on our interim analyses. Yes, I am sorry, I had to echo Dean there. I think learnings what I was happy to see was consistency of data from sort of the Phase 2 data sets into the OptiTROP-Lung05, including, as you get into bigger studies will safety be the same, and we saw very consistent data.

And so that's sort of -- you think about: How do you take that kind of information? This is also not the first Phase 3 that we have from our partners. They've had multiple Phase 3 readouts. And so we're seeing consistent data across multiple indications with the AE profile, with the dose modification, with the discontinuation.

And that is how we have learned in our global studies to be able to ensure that AE management is as tight as possible. Physicians are so good at learning how to manage toxicities over time. But in global studies, we don't want them to have to learn in real time because it puts the patient in a bad spot and our ability to show a benefit at a disadvantage. And so that information has informed for how we are overseeing and how we're managing our Phase 3 programs.

Peter Dannenbaum - *Merck & Co., Inc. - Senior Vice President, Investor Relations*

Vamil?

Vamil Divan - *Guggenheim Securities LLC - Equity Analyst*

Vamil Divan from Guggenheim. So two for me. So one, obviously, you laid out a lot of -- what you've done to diversify away from KEYTRUDA. Just curious if you want to comment more on kind of where you see openings to further diversify, whether it's modalities, mechanisms based on -- was it ASCO or just more generally? And feel free to take that outside of oncology, if you want to.

And then just the second part is just around the -- obviously, a lot of interesting data from China. You guys are taking advantage of this. Just how were thinking of balancing, I guess, obviously a large U.S. biopharma Company, how you're balancing sort of leveraging the speed of development in China, but also investing in the U.S.

I think a lot of concerns raised here around what this means for the U.S. biopharma industry. So any comments you want to make there?

Dean Y. Li, M.D., Ph.D. - *Merck & Co., Inc. - Executive Vice President and President, Merck Research Laboratories*

So I'm going to take your last question because I heard that completely. I think that China is an important player, and we've recognized that. I mean, I just -- our partnership with Kelun is not just about assets, it's about their people and how they think. And we're very lucky to have that collaboration.

And we have recognized that, and I can't remember when it was publicly disclosed. Maybe it was publicly disclosed in '22, something like that, but we have worked with them longer than that. And so we have enormous respect for what they do.

But I also want to just emphasize that there are so many important things that are happening outside of China. And I would just emphasize, for example, there is a possibility that for the first time after, I don't know, three, four years, it could be, quote-unquote, a cancer vaccine does -- and I don't mean hepatitis B, GARDASIL, or EBV. I mean that. And that's something that we're extremely lucky to be partnered with Moderna.

So I just want to make sure that that's emphasized. And then when you look at -- you guys talked about the KRAS space. You have to give credit to, for example, Amgen and Mirati. They pioneered that with Switch 2. And you have to give incredible kudos to the work done from Rev Med using a tri-complex inhibitors.

So for us, it's important to take innovation from the best places throughout the globe. And I hope that we continue to do that because these diseases take more than one bright idea. So that's where I would lay that question is.

What was the first?

Peter Dannenbaum - *Merck & Co., Inc. - Senior Vice President, Investor Relations*

Part one was other areas within oncology that you might consider moving into?

Dean Y. Li, M.D., Ph.D. - *Merck & Co., Inc. - Executive Vice President and President, Merck Research Laboratories*

So one is the heme. We just want to make sure you guys realize we're making an array in heme. And I'm not sure if he's listening, but it's a little bit of a homage to Roy Baynes, who's a heme malignancy who was stuck doing a whole bunch of solid tumor stuff and did a pretty reasonable job, if I may say so.

But this is a bone marrow transplant heme malignancy guy. So if we're successful with this, I hope that he will eat at a burger joint with me, and I will give him enlicitide. But that's a place.

But the other place is tissue targeting. We think tissue targeting is really important. We talked about antibody drug conjugates. We talked about Kelun, we talked about Daiichi Sankyo, but we have not revealed the internal pipeline that is moving fast.

Tissue targeting is not just with a chemo payload. There's other payloads that you can do. And increasingly, the work -- actually, you have to give Roger Perlmutter some credit at a different Company who was very much advancing T-cell engagers largely in heme malignancy, but there's been a corner turn with T cell engagers in solid tumors.

So you see it in our -- right? We look at KEYNOTE-189 and play and sit there and go, that's great. But for small cell lung cancer, what you see is that we're trying to do KEYNOTE-189 there. How we're trying to do it? We're trying to use a next-gen chemo with an ADC and the next-gen IO with a T cell engager. And if that works, we wonder how broad that principle is in places where maybe pembro didn't work as well as we had hoped. So those places are really important to us.

Peter Dannenbaum - *Merck & Co., Inc. - Senior Vice President, Investor Relations*

So I know there's still a few hands going up. We may be able to remain here for a few minutes after we're done to answer any follow-up questions, but we'll end with Meacham.

Geoffrey Meacham - *Citibank - Analyst*

Meacham from Citi. On your broader ADC strategy, given sector MDs studied across various indications and assuming it moves into earlier lines across different tier indications, how do you think about downstream treatment sequencing with your other ADC, especially TROP2 ADCs?

Just trying to get a sense of your internal framework for avoiding ADC overlap across targets, payloads, or tumor indications.

Dean Y. Li, M.D., Ph.D. - *Merck & Co., Inc. - Executive Vice President and President, Merck Research Laboratories*

Yes. I mean, I will give it to Marjorie. But every time you come up with a therapy as great as KEYTRUDA, number one is not everyone responds, right? And the other second thing is you can respond and then not respond. So it's almost like an incessant need for constant innovation.

So with that, I'll turn it over to Marjorie.

Marjorie Green - *Merck & Co., Inc. - Senior Vice President, Head of Oncology, Global Clinical Development*

Yes, I think this is why we have such an extensive biomarker program in our sac-TMT program as well as in our other targeted therapies is that it is -- because of antibody drug conjugates as one example and here what you've asked about, have multiple ways that they can work through bystander effect through sort of the differences in the payload, the DAR, there are going to be differences amongst all of these drugs.

And so some of them may need to have specific enrichment to get to where you may want to use drug A versus drug B. I think it's to be determined how these will separate at what time. We've already seen some antibody drug conjugates approved to have biomarkers, like in ovarian cancer, wherever that has happened, and we've seen them in bladder where it doesn't.

So I'm not going to speculate on the future. I think it is important to understand where people are most likely to have benefit and least likely to have detriment. And that will help separate out how these drugs work over time, is the general guess.

There's very immature data about the ability to sequence antibody drug conjugates. There are some -- there are small data sets looking, for example, at the Daiichi's great DXd platform showing that there is less response. When you do, for example, in HER2-positive breast cancer, one into the next. It doesn't mean that, for example, like a Kadcyla couldn't work, but the same payload may have some challenges.

And I think that there is a lot of interest in thinking about what is the mechanism of resistance? Is it topoisomerase kind of mutation? Is it pump? Could you change the payload to where the pump doesn't kick the payload out?

And that will help with the sequencing part. This is true just like with chemotherapy itself is that we generally don't give taxane one straight into taxane two for most tumors. There are some kind of brakes in payload switching or chemotherapeutic switching. And I think the same thing will be true for ADCs. I'm speculating, though.

Peter Dannenbaum - *Merck & Co., Inc. - Senior Vice President, Investor Relations*

All right. Thank you all again for your time and attention and some really great questions. We appreciate it.

Dean, anything you'd want to close with?

Dean Y. Li, M.D., Ph.D. - *Merck & Co., Inc. - Executive Vice President and President, Merck Research Laboratories*

Please enjoy. There's bacon in the back. And enlicitide, we hope, will be available shortly.
