OVERVIEW:
Company Summary
Thank you for standing by. Welcome to the Merck & Co., Inc., Investor Event at the American Society of Clinical Oncology Annual Meeting. (Operator Instructions)

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 - SVP, IR
Thank you, Julie. Good evening, everyone. Welcome to Merck's Investor Event here at the American Society of Clinical Oncology Annual Meeting, and thank you to all of you that are in the room here with us tonight and to all of you tuning in via the webcast. Thank you. Thanks for your attention and the effort you made to get here.

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. It's been posted to the Investor Relations section of Merck's website.

And before we get started, we'd like to remind you that some of the statements that we make during today's call may be considered forward-looking statements within the meaning of the Safe Harbor provision of the US Private Securities Litigation Reform Act of 1995. Such statements are made based on the current beliefs of Merck's management and are subject to significant risks and uncertainties.
If our underlying assumptions prove inaccurate or uncertainties materialize, actual results may differ materially from those set forth in the forward-looking statements. Please reference this slide in our presentation and our 2023 10-K, which identifies certain risk factors and cautionary statements.

It’s now my pleasure to introduce Dr. Dean Li, President of Merck Research Labs, who will make a few opening remarks and outline our agenda and speaker lineup. Dean?

Dean Li - Merck & Co Inc - Executive Vice President, President - Merck Research Laboratories

Thank you. Thank you very much for all of you for being here, and thank you, Peter. It’s a pleasure to be here with all of you in the room and also all of you who are here virtually as well.

This evening, what we intend to do is provide an overview of our ongoing progress across a diverse oncology pipeline and our strategy for enduring leadership in oncology. First, I will seek to orient us to the significant progress we’ve made since the executive leadership transition that occurred throughout the first half of 2021. Next, we will have Dr. Eliav Barr, Head of Global Clinical Development and our Chief Medical Officer, who will provide an overview of our oncology strategy and then an update on our progress in earlier-stage cancers and how we are leveraging our foundational position in immuno-oncology to improve outcomes for patients.

Then, Marjorie Green, Senior Vice President and Head of Late-Stage Oncology Development, will provide an update on our tissue-targeting strategy, most notably our broad ADC portfolio, and our progress across multiple precision molecular targeting agents. And then finally, Chirfi Guindo, our Chief Marketing Officer and Human Health, will provide an update on the commercial landscape and the opportunity we see to further impact patient lives. After that, I’ll have a few closing remarks prior to opening it up for Q&A.

So as we have spoken many times, we have built on the great foundation set by the preceding leadership team and made significant progress to leverage Merck’s position with KEYTRUDA to create a diverse pipeline that positions us well to achieve and maintain leadership in oncology. And I’m pleased to report, as shown in this slide, that since the beginning of 2021, across our oncology portfolio, we have increased the number of approved indications from 40 to 53, the number of approvals in earlier-stage cancers from 2 to 10, and the number of late-phase candidates being studied in combination from 2 to 9. While this is important progress, we intend to further build upon each of these metrics in the ongoing future.

Today, KEYTRUDA is the only PD-1/PD-L1 to have received nine US approvals in earlier-stage disease. And importantly, KEYTRUDA is the only PD-1/PD-L1 to date to demonstrate a significant OS benefit in any earlier-stage cancer. KEYTRUDA has demonstrated an OS benefit in four earlier-stage tumor types, non-small-cell lung cancer, RCCs, cervical cancer, and most recently, in TNBC, triple negative breast cancer.

Now, achieving OS in earlier-stage disease sets an evidentiary high bar that differentiates us from the competition. We continue to build on this momentum by executing on our strategy and diversifying our pipeline across three strategic pillars -- immuno-oncology, precision molecular, and tissue-targeting agents -- and Eliav and Marjorie will provide more details on the exceptional progress we have made across each of these areas.

And with that, I’ll turn it over to Eliav.

Eliav Barr - Merck & Co Inc - SVP, Head of Clinical Development & Chief Medical Officer

Great. Well, again, thanks everyone for coming at this late stage in ASCO. I’m sure all of you have had a great meeting. And it’s great to be here to give you an update on our oncology strategy and our portfolio.

So as Dean noted, our investment in trials of KEYTRUDA in early-stage cancer continue to bear fruit. We anticipated really important readouts over the next few years in early-stage cancers. And I think that they’ll be an important set of milestones that will guide us in our future with our new diversified pipeline. These readouts will improve not only patients’ outcomes with KEYTRUDA, but as I mentioned, as we move forward and you’ll
see our diverse pipeline, we're already starting to use some of the KEYTRUDA learning to build a platform on which we can further help patients with their disease in the early stage.

So we're going to talk a little bit about the company's journey over the past few years. We're moving from a singular emphasis on immunotherapy to a portfolio that encompasses multiple mechanisms of action, novel combinations, and work with responder populations as we think about biomarkers.

Our goal really is to find the right medicine for the right time -- at the right time in the right stage of disease. We’d like to have a focus that includes both metastatic and now earlier-stage cancer, where there's a potential for a cure. So we're really excited about that. And of course, we're working through every part of the spectrum of cancers. Our early cancer platforms have created new opportunities to provide patients with the right treatment based on the risk of recurrence.

We're also continuing our work in the metastatic and late-line and advanced and operable settings. These patients still have a lot of unmet need, even though pembrolizumab has really been transformative. And then finally, until recently, we focused on KEYTRUDA and a few other agents.

Now, we see KEYTRUDA as part of a broad and deep toolbox of a diverse range of medicines, and we're going to be able to leverage the KEYTRUDA database to evaluate these new populations of unmet need, as well as the new agents that we have in our pipeline.

I think that what's also exciting about the pipeline now is that we're going to have new candidate drugs, such as opevesostat and zilovertamab vedotin, which will enable us to reach cancers that have not been heretofore responsive to immune checkpoint inhibitors, including KEYTRUDA.

So I think that's going to increase the spectrum of cancers that we will be able to help patients with.

Now, our oncology pipeline can be divided into three pillars. The first pillar is immuno-oncology, and that's led by KEYTRUDA, of course, and now V940. Within the pembrolizumab world, we anticipate readouts for MK-3475A, which is the subcutaneous pembrolizumab combined with hyaluronidase, which has the potential to improve patient's treatment journeys, to enhance patient access, and to improve the flow of patients through the oncology outpatient clinic.

We continue to build on the Phase 3 and translational programs for V940, our individualized new antigen therapy, to define the scope and the opportunity for this really promising innovation which we have in collaboration with Moderna. We also, of course, have a number of fixed-dose combinations that combine pembrolizumab with other immune checkpoint inhibitors, such as TIGIT, CTLA-4, and LAG-3. These agents are well into registration trials and will read out in the next one to two years.

Now, the second pillar is our precision molecular targeting medicines, where we have three licensed and four investigational medicines. Each of these agents, I think, offers unique advantages. For example, belzutifan is the first and only licensed HIF2-alpha inhibitor. It promises to improve outcomes in certain patients with RCC, where KEYTRUDA has been foundational for care. And you see a rather substantial program for that drug across the spectrum of renal cell cancer.

Opevesostat offers the possibility of complete steroid hormone blockade with potential applications in prostate, breast, and other hormone-sensitive tumors. MK-1084, which is a potent KRAS G12C inhibitor that is compatible with KEYTRUDA and standards of care, allows us to have opportunities across the spectrum of KRAS G12C-positive cancers.

And finally, we, of course, have the third pillar, which is our tissue-targeting medicines. That includes our broad investigational ADC pipeline that enables us to attack a whole variety of cancers -- a diverse set of cancers, including different histologies and different driver mutations, different disease stages, and different standards of care.

We also have our investigational T cell engager that has opened new horizons, as well as a pipeline behind it from the acquisition of Harpoon. And speaking of this pipeline, we think we have an active in-house pipeline that's going to deliver novel iterations in all of these agents. So overall, our inline and pipeline medicines have the potential to address a broad range of cancers, either monotherapy, in combinations with standard of care, but also in combination with each other to create bespoke, highly specific regimens that we hope will really transform care for several cancers.
Now, we and our partners have advanced 14 different oncology candidate medicines into Phase 3. And that number undercounts the novel combinations, of course, that we have -- we anticipate may potentially enhance efficacy in specific populations, again, in those that include those where KEYTRUDA has not shown particular efficacy.

Now, as we've pivoted to the new era, we've made use of our unique operational capabilities. This is a really important tool that I'm very proud of that has enabled us to enroll with very high quality throughout the COVID era and in a whole diverse set of tumors without missing a beat. And of course, our biomarker team continues to make advances in delivering responder populations. These, I think, are going to become more and more important as we build these sophisticated combinations that we hope to be able to really improve outcomes for targeted sets of patients.

So as we look at our progress, we have listed over 30 new late-phase oncology trials in clinicaltrials.gov. We are nearing the PDUFA date for patritumab deruxtecan, which is our HER3 ADC that's partnered with Daiichi Sankyo. We anticipate that MK-3475A, which is that fixed combination of pembrolizumab with hyaluronidase, will be used in future trials aimed at outpatients, and the results of the Phase 3 program for that should be available in the not-too-distant future. And as the year progresses, we'll have more and more diversity in the medicines for which we are starting in registrational trials. Many of these will be antibody drug conjugates and a bunch of the targeted agents that we’ve talked about just now.

So let me just focus for a second on early-stage cancers. You've heard a little bit about this from Dean. We've enrolled approximately 30,000 patients over 30 Phase 3 clinical trials in early-stage cancers. The investment in these studies spans many years because these studies tend to be quite long to enable demonstration of overall survival benefit.

The investments are now reading out, and this should be really exciting for patients and for their providers. We've amassed 10 approvals in early-stage disease, and this includes melanoma; two different settings in early-stage lung cancer, both adjuvant and perioperative; renal cell cancer; non-muscle-invasive bladder cancer; triple-negative breast cancer; and most recently with KEYNOTE-A18 in cervical cancer, locally advanced but operable.

KEYTRUDA has not only laid the foundation as an immunotherapy option in treating cancers, but it's also the only iotherapy to demonstrate overall survival benefit in four early-stage cancers, which are shown in this slide. KEYNOTE-671 has really been a landmark study because it demonstrates an overall survival benefit in resectable non-small cell lung cancer, and we have a 28% reduction in the risk of death with the administration of KEYTRUDA. KEYNOTE-564 represents the only IO study to demonstrate an overall survival benefit in the adjuvant treatment of renal cell cancer post-surgery, and there, we show that KEYTRUDA reduces the risk of death by 38%.

And then, we've just announced positive results with KEYNOTE-A18 in cervical cancer and, most recently, just last week, KEYNOTE-522 in triple-negative breast cancer, which is, for me, a really exciting moment in our advance to improve outcomes for women with cancer. OS results for those studies have not been -- the actual OS results have not been yet publicly disclosed, but we are working hard to get it at upcoming conferences, and I'm sure that you'll be excited by the results as we are.

The unprecedented benefit of pembrolizumab across multiple tumor types in early-stage settings further reinforces our belief that we have a real opportunity to delay or prevent near-term relapses and with a goal of treating more and more patients and more cancers and allowing patients to have longer lives.

Now, of course, KEYTRUDA is not a cure. It improves outcomes in patients, and there's room to improve outcomes even further, especially those with continuing high risk. We've been able to interrogate the KEYTRUDA studies to define specific populations, specific places where we can properly utilize our new pipeline of various kinds of medicines and to try to lower the risk of patients at high risk while, at the same time, not over-treating patients who are at low risk. And I think our pipeline is pretty good -- pretty well suited to optimize therapy in early cancer.

Candidate medicines have different mechanisms of action, safety profiles, and punitive enrichment biomarkers to guide future research efforts. So if you look at our non-small cell lung cancer research program involving a lot of our assets, you can see how we're moving from, for example here, KEYNOTE-091 to the next generation of studies.
So we’re studying several agents here. V940, of course, is a personalized anti-cancer therapy vaccine – well, anti-cancer therapy, not quite a vaccine. Administration of V940 with pembrolizumab in early lung cancer has been shown to induce tumor shrinkage or stabilization. So we’re excited about that.

This combination has better tolerability than many chemotherapy-based regimens. So we’re initiating studies in early lung cancer to evaluate V940’s potential there. And so this will be an opportunity to see whether we can really change and increase the disease-free survival for patients over the years after adjuvant therapy.

We also have our ADC candidate 2870, now called sac-TMT. And in the perioperative setting, certain patients remain at high risk for recurrence even after they’ve had the benefit of KEYTRUDA. These patients can potentially benefit from more intensive therapy while avoiding the level of treatment intensity for those patients who don’t need it. So if you look at the KEYNOTE-671 example, we have patients who have achieved pathologic complete response and those that have not. And so the idea here with MK-2870 is those patients who have not achieved pathologic complete response and have very high event rates, even with KEYTRUDA, which improves outcomes quite a bit in this population, now, we can add 2870 and hopefully improve their outcomes for there.

The same is true in adjuvant treatment of renal cell cancer where we have different approaches to improve outcomes in patients. You can see that we have studies with either belzutifan or V940. Belzutifan has now been shown to benefit patients in later lines of the renal cell cancer, and now, we’re testing it in the adjuvant setting.

The V940 study is a very important study in the history of our work in V940 because RCC is pembro-responsive but has a relatively lower tumor mutational burden compared to the other tumors that we’ve done most of our primary work there. And so we anticipate that the results of the study will demonstrate that we can expand the utility of V940 across levels of tumor mutational burden and be able to use this to prevent patients from getting relapsed. Of course, V940 is being evaluated in melanoma as well in the very highly mutated cancers like cutaneous squamous cell cancer.

We’re also interested in expanding the benefit we’ve seen with KEYNOTE-522 to address triple negative breast cancer patients who continue to have poor outcomes, and we hope that their intensification of therapy will help certain patients who still remain at high risk.

And finally, we continue to be impressed by the efficacy and safety profiles of pembrolizumab and V940 observed in KEYNOTE-942. Here at ASCO, we reported on the durability of efficacy of the combination, and this is very important. So KEYNOTE-942 study has recurrence-free survival rates that are consistently now at 0.5. The regimen continues to demonstrate robust results for prevention of distant metastasis, as well as a favorable trend for overall survival, although the numbers are pretty small.

The durability of efficacy is very important because this is an INT. It’s meant to reset the immune system to a different trajectory of being able to control the cancer, and so not seeing late recurrences is a very important landmark for the utility of this product. So the curves that we see are really encouraging for us.

And again, it will be important to see what other ways we can use V940. I think they were right at the beginning of a very long exploration as we improve on this modality and look to see whether there’s situations where we might use V940 alone, for example, without pembrolizumab. We’ll see.

And with that, I’ll turn it over to Marjorie, who will speak about some of the tissue-targeting and precision medicine tools in our pipeline.

Marjorie Green - Merck & Co Inc - SVP, Head of Oncology Clinical Development

Thanks, Eliav. Hi, everybody. Good evening. I'm excited to talk to you about a few key areas of focus in our oncology program, and I'm going to start first with ADCs.
We've made very strong progress in building our ADC portfolio over the past few years. We've assembled one of the strongest pipelines of ADCs currently in clinic through our collaborations with Kelun, as well as Daiichi Sankyo. We have targets that are differentiated, either with the potential to be first in class or have the opportunity to be best in class through the assets themselves or how we're developing them.

Part of the potential of our ADC portfolio in relation to the change of standard of care is the potential for combinations and particularly with KEYTRUDA. As Eliav has outlined, KEYTRUDA has become foundational across multiple malignancies. And when you look at the scope of the data that he showed, not only in the metastatic setting, but going into the curative setting, you have to have therapies that are better than those combinations.

Chemotherapy previously was considered what you had to improve upon and beat. And ADCs are better chemotherapies and better ability to deliver cytotoxic at this time. By having the detailed knowledge of these studies and laying the groundwork with KEYTRUDA combinations across multiple therapeutic areas, we're able to combine our ADCs with KEYTRUDA in ways that have the potential to be clinically very meaningful to patients and physicians.

So an example of this that I think got everyone really excited was the KEYNOTE-A39 data, which really demonstrates the power you can have combining an ADC with KEYTRUDA. This study in the locally advanced or metastatic urothelial cancer population significantly reduced the risk of progression or death. The reduction of death was 47% in a disease where there had not been an improvement in more than 20 years and, I think, five or six negative Phase 3 studies before this trial. So when you see this kind of data, it's really exciting and it highlights the potential of what we can see combining ADCs with checkpoint inhibition with KEYTRUDA.

We assess each of our ADCs individually, and we're very aware of the data that comes out through our competitors, as well as the data that we generate internally. And what we try to do is provide value for patients and clinicians by seeing where can we optimize monotherapy, where can we be first, either in the types of studies we do or the way that people practice the medicine, and where can we have novel treatment approaches and novel combinations.

And so as an example, with MK-2870, sac-TMT, as you look at the development program that we publicly disclosed to date, there are a variety of different approaches. And we have created a development plan that reflects the unique characteristics of this asset while recognizing we're bringing medications forward in a very competitive and increasing fragmented treatment landscape. So we're excited by what's going on with sac-TMT.

And one of the things that excites us is the data that Kelun has been generating and moving forward. So at this meeting, you saw data where Kelun conducted a Phase 3 study in the third line plus triple receptor negative breast cancer setting, comparing MK-2870, sac-TMT, versus treatment of physician's choice. This was done in a primarily Chinese population. And when comparing sac-TMT to standard of care chemotherapy, sac-TMT had a clinically meaningful improvement in progression-free and overall survival.

So it's really rare for us to have data like this when we're so early in our global development planning. And so this gives us great confidence in the characteristics of this medication as we are developing and initiating our Phase 3 studies. We have multiple Phase 3 studies underway, and we have more to come.

In addition to MK-2870, we are advancing three potentially first-in-class ADCs. These are being co-developed as part of our collaboration with Daiichi Sankyo. We have MK-22, which is a HER3-DXd. As you all are aware, this has received priority review for HERTHENA-Lung01. Our PDUFA date is at the end of June. We have studies ongoing not only in non-small cell lung cancer but in breast cancer.

Next, we have MK-2400, or I-DXd. This is a B7H3-targeted ADC. There is expression of B7H3 broadly across multiple tumor types. We've shown very encouraging data in small cell lung cancer and Phase 3 programs that are already underway there. But there is activity and evidence of a potential promise across multiple malignancies, including esophageal squamous carcinoma, prostate cancer, and non-small cell lung cancer. So we have significant opportunity for development with this asset as well.

Finally, we have MK-5909, which is R-DXd, which is a CDH6-targeted ADC, showing very promising efficacy and activity in patients with heavily pretreated platinum-resistant ovarian cancer. We have initiated a Phase 2/3 study based upon the promise of this early data. And so for each one
of these ADCs, as well as the ones I haven’t talked about, that same thought and rigor that goes into the development plans because we want to ensure we can optimize benefit for patients and for providers.

Our tissue-targeting portfolio has grown further with the acquisition of Harpoon Therapeutics. Harpoon Therapeutics specialize in development of T cell engagers. The T cell engagers take the power of an antibody to bring T cells directed to tumor cells and are differentiated from CAR-Ts and other cellular-based therapies that they have the potential to be given off the shelf.

This acquisition brings MK-6070 into the portfolio. This is a DLL3-targeted T cell engager that has shown clinical activity in small cell lung cancer, as well as in other neuroendocrine tumors. It’s been a very thoughtfully designed platform by Harpoon to minimize non-specific T cell activation and systemic toxicities and also to improve the half-life of the medication. We look forward to advancing this molecule with the hope to help more patients.

Harpoon’s lead asset, MK-6070, has demonstrated very promising data in small cell lung cancer, as well as neuroendocrine tumors. Small cell lung cancer remains a disease with significant morbidity and mortality and huge unmet need, so we’re excited to have two different assets in the portfolio that work quite differently that potentially will bring promise to this very, very high unmet need disease. We’re excited about both of them, and our goal is to provide options to patients and address the high unmet need that exists in this disease state.

Continuing in lung cancer, specifically in non-small cell lung cancer, we have initiated our first Phase 3 trial evaluating MK-1084, which is our KRAS G12C inhibitor, in combination with pembrolizumab. This is the potential best-in-class orally bioavailable KRAS G12C inhibitor that targets G12C-mediated signaling. It’s designed to maximize the efficacy of the drug while minimizing toxicity as monotherapy as well in combination.

In non-small cell lung cancer, a combination of therapy has been the cornerstone of treatment. Notably, KEYTRUDA and KEYTRUDA combinations have demonstrated an ability to combine therapy without modulating or minimizing the doses of the core drug, and that’s been critical to achieve efficacy and patient benefit. The combination of MK-1084 and pembrolizumab has robust activity, as you see in the slide, in early clinical Phase 1 studies. Patients who have tumors who have high PD-L1 expression response rates are in the 75% range.

Efficacy is always the goal for the patients who’ve got metastatic disease and have very, very poor outcomes, but we also have to be worried about tolerability in the patient profile and the therapeutic index. In early days in these Phase 1 studies, we’ve had minimal modification of 1084 dosing in combination with KEYTRUDA with very manageable toxicities, and so we’re excited about this Phase 3 study, and this is the first of many to come.

Finally, moving into precision molecular targeting, I want to speak about WELIREG, which I don’t think always gets the love that it maybe deserves. WELIREG is a HIF-2 alpha inhibitor that’s been approved in the United States for treatment of adults with certain DHL disease-associated tumors. The mechanism of action has sort of its angiogenic adjacent, dealing with oxygenation. In LITESPARK-005, WELIREG demonstrated an improvement in progression-free survival for patients previously treated advanced renal cell carcinoma.

And as you see on this slide, we have multiple studies that are underway looking at WELIREG, building upon the successes we’ve had with KEYTRUDA, and we’re doing this with many of our medications in our portfolio. So we’re advancing not only in the first-line metastatic setting, but also into the adjuvant setting, building on KEYNOTE-564. We’ve shown an overall survival advantage, and I’m pleased to announce that LITESPARK-022 has completed an enrollment already in the adjuvant setting ahead of schedule. We look forward to providing updates of that trial in due course.

With that, I’d like to hand this over to Chirfi.

Chirfi Guindo - Merck & Co Inc - Senior Vice President, Chief Marketing Officer - Human Health

All right. Thank you, Marjorie. Good evening, everyone. Thanks for coming. Let me just see here.

So as you’ve heard today, we have made significant progress delivering a cross-oncology strategy that we’ve articulated to bring forward new treatment options for patients. We have a strong commercial engine. We have built what we believe to be the strongest engine in the business that has enabled us, our differentiated portfolio, to reach 2.6 million patients globally.
Importantly, our expanding access -- we're expanding access both in the United States, as well as internationally. In the US, we have 53 approved indications across 23 tumor types and two tumor-agnostic indications. Outside of the US, we've also made significant progress, with over 70 indications in the EU and Japan alone. We're confident in our ability to continue this momentum, benefiting more patients and driving growth for the company.

Our growth in oncology is increasingly driven by strong uptake in earlier-stage indications. This is a recurring theme. You've heard it from my colleagues. Earlier-stage indications are going to be a significant driver of growth. To date, we've executed 10 successful launches in earlier-stage cancers across six tumor types. We're already seeing a shift in our KEYTRUDA business to earlier-stage indications as evidenced by the progress we're seeing with KEYNOTE-522 in triple negative breast cancer and KEYNOTE-671 and KEYNOTE-091 in earlier-stage non-small cell lung cancer.

In the US, we've achieved strong growth with encouraging signals. In earlier-stage non-small cell lung cancer, for example, treatment rates have increased from 35% to 65% since we launched KEYNOTE-091. We've seen continued uptake in high-risk early-stage TNBC, where the adjuvant treatment rate has now reached 65%. We have a differentiated portfolio, with KEYTRUDA being the only IO, as Dean showed earlier, to date that has demonstrated a significant overall survival in earlier-stage cancers. We have four. This is important for patients, it's important for physicians, and increasingly for payers as well.

Outside the US, we're encouraged by countries’ continuous willingness or increasing willingness to reimburse based on the strength of our data. In many of those countries, the OS benefit is, in fact, an important consideration for reimbursement.

Globally, in 2023, earlier stage represented 20% of our overall KEYTRUDA revenue. Due to our strong momentum, we expect this growth to reach 25% by the end of this year, which is ahead of our initial expectations. We expect growth thereafter to continue, driven by uptake from existing early-stage indications, as well as new indications which are currently in clinical development.

Next, I'll cover the significant progress we're making across three key tumor types where we have a strong foundation and line of sight to the next wave of opportunities -- lung, bladder, and RCC. So first, non-small cell lung cancer, we have a broad portfolio of KEYTRUDA-based regimens, both in earlier-stage and metastatic settings.

We're taking a complementary approach to addressing areas of continued unmet need, and we look forward to the potential approval for our differentiated HER3 ADC in collaboration with Daiichi Sankyo in EGFR-mutated non-small cell lung cancer, which has a PDUFA of June 26. This is a first-in-class HER3 ADC, which we believe will also be our first ADC launch, by the way, and we believe it has the potential to be a new standard of care for this population. We look forward, as we are advancing more programs, to evaluate HER3-DXd in earlier lines, as well as in other tumor types, including breast.

Bladder -- we have four approved indications spanning non-muscle invasive bladder cancer and advanced urothelial cancer. Our most recent approval for KEYTRUDA plus PACEV in first-line locally advanced or metastatic urothelial cancer represents the first approval of a combination with PD-1 or PD-L1, together with an ADC, in this patient population.

It has the potential to change the treatment paradigm for a population with a high unmet medical need, and the commercial opportunity in this combination is very significant. Bladder remains a high unmet patient need, and we have additional efforts, including in the earlier-stage settings, reading out over the next several years, which will further extend our leadership in bladder cancer.

In RCC, we believe that the approval of WELIREG has been a significant advancement for patients with VHL-associated RCC and for the patients with advanced RCC following treatment with both PD-1 and PD-L1 and VGF TKI therapies. As a HIF-2-alpha inhibitor, WELIREG is the first new mechanism of action approved in advanced RCC in almost 10 years, and we are already seeing strong uptake in the United States.

Beyond these approvals, we have a robust clinical program to explore WELIREG's further potential in advanced RCC, as well as additional tumor types. We believe that in aggregate, WELIREG has a blockbuster potential.
As you can see, we have a diversified pipeline and commercial portfolio, and we're confident in our ability to maintain leadership in oncology. We believe our oncology pipeline has the opportunity for an incremental $20 billion sales approaching the mid-2030s, excluding the currently marketed products and excluding additional business development. This includes potential contributions from V940, small molecules, as well as the suite of ADCs that Marjorie just showed you. We're confident in our ability to execute commercially to deliver for patients and create value well into the next decade.

With that, I'll hand back to Dean.

Dean Li - Merck & Co Inc - Executive Vice President, President - Merck Research Laboratories

Thank you, Chirfi.

Let me close by saying we're making strong progress as we continue to build on our strong foundation in immuno-oncology, working to advance a bold aspiration with the potential to further reshape oncology treatment. We are expanding into additional tumor types. We are deepening with novel combinations and extending into earlier stage of disease, all of which we believe will improve the impact of the pipeline on patients. We remain confident in our three-pillared strategy and look forward to providing further updates soon.

I'll turn it over now to Peter to begin Q&A.

Peter Dannenbaum - Merck & Co Inc - SVP, IR

Okay. Thank you, Dean. We're now happy to take your questions. So for our Q&A session, in addition to our speakers, we have Joanne Monahan here in the front row with us. Joanne leads Merck's US oncology business.

So we're going to start with questions in the room. We're also going to take a few from the webcast. And Julie, would you please provide instructions for the virtual attendees to get in the queue?

Q U E S T I O N S  A N D  A N S W E R S

Operator

(Operator Instructions)

Peter Dannenbaum - Merck & Co Inc - SVP, IR

Okay. Starting here in the room, so please raise your hand. And when the mic -- Domini and Steve are here with mics, just please state your name and your firm name when they hand you the mic. Maybe Carter.

Carter Gould - Barclays - Analyst

Thank you. Carter Gould, Barclays. The Harpoon data, it looks as though you potentially have a differentiated CRS profile relative to some of your competition. At this point, how do you feel about your confidence to potentially differentiate on that, as well as the logistics associated with the MDELTRA kind of approval?

And maybe sort of a tag on a little bit of a cheeky question, is there an opportunity to sort of resuscitate KEYTRUDA development in front line as you think about combinations here? Or are you going to follow somewhat more of a more boring path and combine with a --
Dean Li - Merck & Co Inc - Executive Vice President, President - Merck Research Laboratories

Well, I would never answer a more boring path, if that's your question. Since it's a question in relationship to IO, I'll have Marjorie take the first shot, and then Elliot can embellish. And we'll go from there. Marjorie?

Marjorie Green - Merck & Co Inc - SVP, Head of Oncology Clinical Development

Thanks for the question. I'm still trying to -- I'm recovering from the boring comment. So we really like the technology of Harpoon which led to the acquisition. And I agree that these are non-comparatives, so we can't say really that the AE profile is different. What we're seeing is very favorable compared to what's publicly available from other assets. And so we're excited about that.

CRS does still happen. And so we're being careful with that. It's early days still for the asset. And so I don't want to get ahead of what we're ready to publicly disclose about our development plans, other than it is -- we really like the technology, EECs through our acquisitions, our BD deals. We're very thoughtful about the approach. We don't want something that may not be first unless we think we can do something really special with it. And so there's a robust development plan that's cooking, and we're looking forward to sharing it as we get more -- as we're ready to do so.

Eliav Barr - Merck & Co Inc - SVP, Head of Clinical Development & Chief Medical Officer

Right. And I think -- first of all, I think that the Harpoon assets are really terrific. And I really think that we're going to have an opportunity to meaningfully impact patients with small cell lung cancer. I'm glad that there are options for patients and that there's already one drug on the market. But I think we have a differentiated way to prosecute the development program for MK-6070.

And you asked that cheeky question about pembroluzumab, but pembroluzumab in small cell never really died. We do have KEYLYNK-013 where we actually are looking at pembroluzumab in limited stage small cell. But in any event, I think that the -- if you look at the suite of products that we have, we have an opportunity to really reset patients' outcomes in small cell, whether it's with 6070 or with l-DXd or with pembroluzumab, comes along and comes back into small cell will be very exciting as well.

Dean Li - Merck & Co Inc - Executive Vice President, President - Merck Research Laboratories

I'll just add one last thing which is, if you look at the tissue-targeting field, especially in relationship to immuno-oncology, clearly, you see tissue targeting if you view CAR-T as a tissue targeting with the cell as a payload has been really important in heme malignancy but has had a harder time moving into solid tumors.

What you see with bispecific immune engagers is you see the bispecific immune engagers, again, starting in heme. But we think this technology has the ability to cross over to solid, and so we're very excited with the Harpoon. But I wanted to give that broader view of how we think about bispecific immune engagers, especially in relationship to solid tumors.

Peter Dannenbaum - Merck & Co Inc - SVP, IR

Chris Schott.

Chris Schott - JPMorgan - Analyst

Great. Thanks so much for the questions. Chris Schott at JPMorgan. Maybe the first question was just on TROP2 and just perspectives there. You obviously are excited about the opportunity. You've got nine studies running now. It seems like competitor data has been more mixed. So I'm just
interested in just elaborating more what gives you confidence to move forward so broadly and so aggressively with the asset. So if you could just elaborate a little bit more on that.

And maybe the second question was there’s some recent headlines on PD-1 VEGF bispecific. Just comment -- is that an approach that you’ve considered? Do you have any perspective on it? And just how do you think about that as a potential competitor/opportunity?

Dean Li - Merck & Co Inc - Executive Vice President, President - Merck Research Laboratories

Why don’t we split it to -- TROP2 ADC, we’ll give to Marjorie, and then the PD-1 VEGF bispecific, because it’s in immuno-oncology, I’ll set to Eliav.

Marjorie Green - Merck & Co Inc - SVP, Head of Oncology Clinical Development

All right. Thanks. I think that there’s a lot of data with 2870 that isn’t public. And so Kelun has been doing a great deal of work, and we have as well, that gives us confidence in the program.

I think as you saw the combination data from the lung study, the OPTITROP1 looking in the first line setting in combination with their PD-1 inhibitor, very robust responses in squamous, non-squame. You see the breast cancer data that they’ve generated, and there’s a lot of data across other tumors.

The ADCs have similar targets, but they’re not identical. And so we do pay attention to what’s going on with [TRODELVY] and with Dato-DXd. But whether it’s the linkers, whether it’s the payload, or combination of the two, as well as your approach to development, there are ways to optimize and differentiate. And so there may be times where monotherapy is going to be fully sufficient, and so we haven’t rushed in necessarily into saying monotherapy in an ITT population is going to win everywhere.

We are being very thoughtful about our biomarker evaluation. So we do think, for some malignancies, it may be needed that you have to have an enriched biomarker strategy. And then the combinations are important for us too. Chemotherapy combinations of ADCs are often quite toxic and problematic. And so we either try to enrich to where we can get the efficacy that we want or in combination, or we try to do a sequencing to where we think we’re going to have benefit. And so that’s why when you look at that development plan, it’s not sort of copy-paste, rubber-stamped, what you’ve seen with the other ADCs out there because they are different drugs, and we are trying to take advantage of the data that we’ve generated and we have understood to go forward.

So we have a lot of confidence in it. We wouldn’t expose patients to medications if we didn’t think that we had a good chance of helping them. And so I hope that you all are excited seeing from the data that is public and out there because it’s just the tip of the iceberg of good stuff to come.

Eliav Barr - Merck & Co Inc - SVP, Head of Clinical Development & Chief Medical Officer

I have to say I agree with Marjorie. These are not the same molecules. These are not the same programs. These are not the same biomarker strategies. And back in the day, there used to be this drug called nivolumab. I don't remember what it does anymore. But anyway -- no, I'm just kidding. But I just do think that there is an opportunity here with a drug that has a specific profile to do the things that we needed to do to help patients.

In terms of the PD-1 VEGF combination, I'm really excited about having options for patients. This sounds really good in the Chinese population. We don't have much of the data. We'll see how it looks.

The situation is such that we -- the KEYNOTE-189 regimen is a very important regimen and one with a very high bar. We're confident that in the long-term efficacy that we've seen with KEYTRUDA, including five-year OS data, and the experience that not only key scientific leaders but community practitioners and the whole spectrum of oncology treaters have had with KEYNOTE-189. So I think that pembrolizumab will have a tremendous role over the course of the next few years. We look forward to seeing what the new data will look like, and we'll make our assessment at that point.
Peter Dannenbaum - Merck & Co Inc - SVP, IR

Evan.

Evan Seigerman - BMO Capital Markets - Analyst

Hi there. Evan Seigerman, BMO Capital Markets. So your big boss recently said that KEYTRUDA is our once-in-a-lifetime drug, and I appreciate that the model is not exactly repeatable as you near the eventual LOE. So what are the three or four most key assets that we should pay attention to as you evolve your business beyond KEYTRUDA as the monolith?

Dean Li - Merck & Co Inc - Executive Vice President, President - Merck Research Laboratories

So I'll let Eliav grab this one. But before, I would say, I think that context, if I'm not mistaken, I wasn't there, but I believe it was in relationship to how policy changes affect how one thinks about medicine. So I want to place that in the context of that.

But with that, I'll first let Eliav go and then I may have some comments that might be reminiscent to some of you when you were here at ASCO two years ago when I made comments in a similar vein.

Eliav Barr - Merck & Co Inc - SVP, Head of Clinical Development & Chief Medical Officer

Sure. So I have to say that if I mention three or four drugs, I'm going to get an earful from every one of my development team leaders. So I need to be cautious. Otherwise, you might be happy, but I'm not going to be happy.

So if I look broad -- if I think with -- sticking within oncology for a second, I think that the -- for me, it's not so much the drugs but the combinations. And I really want that to be clear. It's not just what the individual drug can do, but what we can do in terms of creating a spectrum of new realities for patients that will really improve outcomes, particularly in biomarker-defined populations, whether it's with KEYTRUDA, with other standards of care, or with each other.

And so when you look at something as transformational as V940, we're really excited about that as being something that's going to transform patients' care with early cancer, where there is an opportunity for a cure. If you think about an ADC that really seems to work very well in driver mutation-driven lung cancers like P-DXd, and then we've got precision medicines that also target -- that also work with targeting specific driver mutations, you might think about synergistic combinations that would be really exciting for us to have.

Now, of course, outside of oncology, we've really diversified the pipeline tremendously. I think sotatercept is extraordinary. I'll stop, and I think you'll see over the course of the time how good it is in transforming the care of PAH. You'll see TL1A and tulisokibart and its extraordinary efficacy. And then you'll see something that's near and dear to my origins in cardiovascular, which is MK-0616, which is our oral PCSK9 inhibitor. All of these drugs and many others, you hear me, team, others as well, are really going to transform our pipeline and create, I think, a lot of value for patients, which will turn into value for investors.

Dean Li - Merck & Co Inc - Executive Vice President, President - Merck Research Laboratories

And I just want to recontextualize, I think, the context of Rob Davis's conversation that got a headline, but if you look at the other comments made by Dave Ricks in this, I mean, just imagine a world where you had another agent that was as broadly impactful in oncology and happened to be a small molecule. And you'd ask yourself, could you really develop it in as many broad indications in late stage? And more importantly, would you drive it into earlier stage, which is a larger patient population, where you can do really a lot of good in a situation where policy changes have potentially made perverse incentives? And I think he was speaking in relationship to that, so I just want to make sure that that balance is taken there.
Peter Dannenbaum - Merck & Co Inc - SVP, IR

Great. Akash.

Akash Tewari - Jefferies LLC - Analyst

Thanks so much. Akash, Jefferies. So you've shown really strong data with your CDH6 ADC in ovarian so far. It looks like it's a 60% response rate at what would be your go-forward dose. What is your potential to be able to file with accelerated approval, similar to the path that ImmunoGen took? And would you be going with a biomarker-agnostic approach?

Secondly, can you talk about your path to bridge subcu KEYTRUDA? You have your Phase 3 study reading out soon. Do you have an agreement with the FDA? Do you have to run separate bridging studies in each of the indications, particularly in adjuvant? Or could you actually have a much more expedited path to development? And if so, what would that look like? Thanks.

Dean Li - Merck & Co Inc - Executive Vice President, President - Merck Research Laboratories

So I'll hand the CDH6 to Marjorie and the pembro plus hyaluronidase to Eliav. But I do echo your observation about CDH6 antibody drug conjugates, the response, and also the response in basically a biomarker non-selected patient population, which I think you were right to point out is impressive. Marjorie?

Marjorie Green - Merck & Co Inc - SVP, Head of Oncology Clinical Development

Thanks. Dean gave part of my answer. So the data that's been presented to date was in a non-biomarker selected population. So we have an ongoing Phase 2/3 study that is looking at R-DXd and platinum-resistant ovarian cancer. We don't disclose our regulatory intentions or necessarily our biomarker strategy where we are at this phase in development. But we want to make sure that we optimize value for patients and clinicians. And so there's going to be more to come, but I can't give you full disclosure today.

Eliav Barr - Merck & Co Inc - SVP, Head of Clinical Development & Chief Medical Officer

All right. But for me, it's one of the most exciting of the molecules that we share with Daiichi, and I'm super excited about that.

With regard to subcu, the MK-3475A, the study program that we agree to with FDA will bridge the indications for KEYTRUDA in the solid tumor space. So it's everything. And we have a precedent for that because we did with Q3 week to Q6 week.

Peter Dannenbaum - Merck & Co Inc - SVP, IR

Steve Scala.

Steve Scala - TD Cowen (Research) - Analyst

Thank you. Steve Scala from TD Cowen. Two questions. First, on the KeyVibe-010 stoppage, I'm curious if the vibostimab added to the efficacy on top of KEYTRUDA, but also added to tox, and that's why the study was stopped. Or did it not add anything in terms of efficacy on top of KEYTRUDA? And if the latter, then why persist with such a widely disappointing target?
And then secondly, other companies have provided views on the percent of patients that could ultimately be on a subcu PD-1 or PD-L1. I don't believe Merck has. Would you say that it's highly unlikely that 50% of patients on KEYTRUDA would be on a subcu version down the road? Thank you.

Dean Li - Merck & Co Inc - Executive Vice President, President - Merck Research Laboratories

So let me just make sure -- the KeyVibe, I'll give to you. I'll let then Chirfi talk about the subcu, and then I may add a comment at the end.

Eliav Barr - Merck & Co Inc - SVP, Head of Clinical Development & Chief Medical Officer

So KeyVibe-010, the toxicity essentially masked any efficacy, but it was very -- I really am not able to discern whether there's any impact on our -- whether we could tell what was going on from the efficacy point of view because there was quite a few discontinuations early on for a variety of toxicities in this patient population that was relatively younger and probably also was not as willing to tolerate some of the adverse experiences that occur with immuno-oncology drugs in general.

I don't see any read-through to the KeyVibe program in the lung space because they're in metastatic patients and it's a very different data set. Not to mention the fact that data monitoring committees have been very actively looking at all the data throughout the course of those studies, and we've not heard any issues around that.

That said, these studies are ongoing. They're enrolled, and we'll just have to see how those data are going to read out. We'll see. Time will tell.

Dean Li - Merck & Co Inc - Executive Vice President, President - Merck Research Laboratories

Chirfi?

Chirfi Guindo - Merck & Co Inc - Senior Vice President, Chief Marketing Officer - Human Health

So just to remind everyone, for us, subcu really is first and foremost about access, about expanding access, both in the United States and internationally, access to patients who have difficulty accessing an infusion suite. So you see that in the rural areas, and you see that in countries such as the UK, where you have an acute shortage of nursing staff. So that's really the starting point.

Now, in terms of demand and our expectations, we can't give you specific numbers, but I can give you an indication of how we are thinking about this. If you think about the source of business going forward, we see an increasing development in earlier-stage cancers. And so those are patients who are most likely to demand, so to speak, a subcu formulation. Patients who are on monotherapy KEYTRUDA and patients who are on a combination with an oral, by definition, those are patients who would be most likely to be kind of the target patient population, so to speak, for the subcu.

We anticipate that you take those together, that they represent approximately 50% of the total KEYTRUDA patient population by 2028. That is not to say that all of those will be on subcu KEYTRUDA. So we estimate that a percentage of those will be on subcu KEYTRUDA by 2028.

Dean Li - Merck & Co Inc - Executive Vice President, President - Merck Research Laboratories

I just want to emphasize in relationship to your question, at least for me, the issue is to create unique situations where we are going to provide an innovation to increase access that's really needed. The reason why I emphasize it is we keep saying that the earlier stage is important, and that's a place where potentially not having to come to an infusion center all the time is quite important. And as someone who practiced in Utah, where it's largely rural, this is a really important point.
The reason I want to emphasize it is that, in the beginning of the discussion, I emphasized how many approvals we have in the earlier stage and how many have OS, and I hope that trend continues because that trend is what’s going to drive the need, the demand for that access. Because if I were someone who was relatively in a curable situation, I don’t want to be going to an infusion center at a major medical infusion center every three weeks or every six weeks. So I want to make sure that when we talk about subcu with pembro and hyaluronidase, we are trying to drive an innovation, and what we’re trying to do in these clinical plans is to try to create a demand for it that’s real and tangible.

Peter Dannenbaum - Merck & Co Inc - SVP, IR

Chris Shibutani.

Chris Shibutani - Goldman Sachs - Analyst

Thank you. Chris Shibutani from Goldman Sachs. Two questions, if I could. On the KRAS G12C, I couldn’t help but note the inflection on the statement about something that is compatible with pembro. Can you talk a little bit more about what is the attribute that you believe that would be the case? There’s often talk about first-line lung and tolerability as being one of the limitations there.

Secondly, it was a year ago at this meeting, immediately following that Merck was the first to step forth and challenge the IRA. In the past year, can you perhaps share any comments since this is a discussion of strategy, how perhaps -- what’s been playing out so far may be shaping or influencing your clinical development strategies? Thank you.

Dean Li - Merck & Co Inc - Executive Vice President, President - Merck Research Laboratories

So I will give the KRAS G12C to Marjorie, but I will have to make a comment because it was at your conference that I talked about KRAS G12C a number of times. And then in terms of development of drugs, I'll quickly ask Eliav that sort of question. I may make a free comment afterwards after that. Marjorie?

Marjorie Green - Merck & Co Inc - SVP, Head of Oncology Clinical Development

So definitely, as Dean was head of our discovery group for a while and has great love for this molecule as we do as well, and so it was very much optimized and designed to have all the key attributes that you need for inhibition while trying to -- it doesn’t have drug-drug interaction. You don’t have the same kind of baseline toxicity with it. It’s very potent, so you’ve got lower overall dose that you’re giving compared to some of the ones that are already out there in studies.

And with that, you’re able to combine in a way that minimizes sort of overlapping toxicity and the risk of the grade 3 higher toxicities, particularly hepatic toxicities. And so we’ve seen in the past there’s some tyrosine kinase inhibitors for different combination with KEYTRUDA could cause some issues. And we’re not having that same issue with 1084 combined with KEYTRUDA. And so that’s what we’re so excited about. It was very thoughtfully designed trying to maximize the potency while minimizing any interactions that exist.

Eliav Barr - Merck & Co Inc - SVP, Head of Clinical Development & Chief Medical Officer

And I would just add to that that the proof of the pudding is that we’re already in Phase 3. And if you note, that’s a pretty fast start in the front line. And we’re going to see more frontline data -- more frontline studies moving forward quickly. This is a drug that combines nicely with KEYTRUDA, period.

In terms of the IRA and how it’s changed drug development for us, I think that Dean just talked about -- imagine if KEYTRUDA were a small molecule and you wanted to develop it to maximize its benefit for patients, it’d be just really hard to do that. And so we’ve tried to frontload a lot of studies that have longer term -- that require longer-term outcomes.
A good example of that is MK-0616. You see that CORALreef outcome study is enrolling very rapidly, and we need to move that up as much as possible. You know how it's going to turn out. Otherwise, we'll be on a drug-by-drug basis.

We are considering -- you just talked about 1084, it's another good example. Because of the platforms that we have that I talked about and the deep knowledge and the ability to select the right patients for the studies, we can bring this drug into various settings that I don't think it's going to be easy for others to bring into. And again, that enables us to try to frontload a lot of the work so that readouts can come in a timeframe. That way, we can have some value for patients while also maintaining the kind of return that will allow the next set of innovations to be possible.

Dean Li - Merck & Co Inc - Executive Vice President, President - Merck Research Laboratories

I would just make two comments, one related to KRAS G12C but probably more broad. In a world that we see in combinations, especially combinations of multiple classes of drugs, we laid out immune, precision, antibody drug conjugates, and this. I think one of the issues is the more you combine, the more efficacy you could get as long as you don't compound adverse effects.

So this issue of having potent molecules that allow you to do that with the aid of adverse effects, it isn't that you're trying to reduce just tolerability which is important for a patient. But it's also when you don't have that, you can't keep the patient on at the appropriate dose. And then you are going to damage your efficacy.

So I got asked this question, if you have a KRAS G12C with a reactive covalent inhibitor, that thing is a hot poker. You have 1,000 milligrams, the chance that that hot poker is going to do something not so great is potentially high, and you worry about in combination liver. If you can reduce it by tenfold, then all of a sudden, you have fewer hot pokers laying around and there's a hope that you're not going to burn your liver quite as much. That's the sort of explanation I gave I think two years ago. And we're hoping that what we had hoped was the design of this molecule might give that. But combinations that are tolerable are really important because they allow you to get the efficacy because you can stay on the drug.

In relationship to the IRA, lots of things have been discussed. There are a number of legal challenges in relationship. But the thing that -- I guess the best way to say it -- bugs me the most is the small molecule penalty. It just does not make sense. In the patient populations that are in the most need of treatment and have the hardest time getting to hospitals and this, those small molecules are the lifeline to really change people's lives. And so I think that deficit is unfortunate.

And when you add on what all of you know, when a small molecule goes off patent, how fast does a generic come in? All of you do the calculation. Is it 15 minutes or 5 minutes in your guys' minds? But for cell therapy, gene therapy, biologics it's not 5 minutes. So it just seems really counterproductive in relationship to those people who are most at risk of not getting treated.

Peter Dannenbaum - Merck & Co Inc - SVP, IR

Trung.

Trung Huynh - UBS Limited - Analyst

Hi, guys. Trung Nguyen, UBS. So I've got one question on Chinese oncology studies and another on V940. So on the Chinese oncology-driven studies, you showed us the sac-TMT data. Over the conference, there was a PR from a biotech called Summit against KEYTRUDA, both of these were exclusively in Chinese populations. Just wondering what's your view of the difference between a Chinese population's efficacy in oncology study versus a global study? Is that something in the Chinese genetics? I'm aware that EGFR is a lot more prevalent in the genetics. Is there anything in the way they run the studies? So just any of your thoughts there.

And then on V940, in the session today, they said that the trial recruited quite quickly or is recruiting quickly. Is that what you're seeing, and could we see that data earlier than the clinicaltrials.gov primary readout?
Dean Li - Merck & Co Inc - Executive Vice President, President - Merck Research Laboratories

So I'll have Marjorie start off with China and then Eliav with his experience more broadly -- this is not just true for oncology, it's more broad take a little bit of the China -- and then make comments about the V940, Eliav.

Marjorie Green - Merck & Co Inc - SVP, Head of Oncology Clinical Development

Thanks. I'll start and stick really to 2870 and talk about sac-TMT and the work that Kelun has been doing. I think that they are a fantastic drug company who's got tremendous experience through their organization and work closely with MSD China and collaboration with investigators in China to enroll a representative Chinese population.

Globally, there's much more ethnic diversity. And so it isn't that the indication of efficacy isn't applicable to what you're going to see globally, but we do need to see across a broad range of different ethnicities sort of how a drug holds up, and global studies are needed to complement and augment what you get in a Chinese-only study. The United States itself is quite diverse, so US-only studies are a little different than ones that are ethnically so uniform that are being done in China.

So we have confidence in the data that's being seen. But is it representative for global access, I think that's where the question comes up because it doesn't reflect the total global population. So we think that we're going to see really good data with sac-TMT beyond the data that's seen in the Kelun studies, and some of the studies actually have been run outside of China only, some of the Phase 1 and Phase 2 studies. So we have some data where we're seeing really good efficacy not only in the China's population but also in other regions.

Eliav Barr - Merck & Co Inc - SVP, Head of Clinical Development & Chief Medical Officer

Right. So thanks for the question. So I think Chinese population studies are important and they have value. Marjorie talked a little bit about the diversity issue, and I think that's important. The other piece has to do with standards of care and what happens after the -- when patients get off drugs.

So a study that has a lot of PFS data, that's great, but then the interval between PFS and OS might be quite different in the Chinese context versus the US context, all depends, on the global context as well. So I don't -- I'm not sure how one can quantify the ethnic diversity bit of it, but it's just the totality of the ethnic plus the different standards of care plus different ways in which AEs may be collected or perceived, plus the need to have different healthcare systems -- and the context of different healthcare systems sometimes can create variability and differences that need to be more careful -- that are best viewed through a global lens.

In terms of V940 enrollment, I've always believed that enrollment rate can be as directly proportional to enthusiasm. And I'd just say that the enrollment rate for V940-001 called INTerpath-001 has really been very nice. It's very rapid.

And one of the things that you didn't ask about but I'll tell you anyway is that I'm just amazed at Moderna's ability to turn around those personalized vaccines. They are not missing a beat. Enrollment is going gangbusters, and so it's lovely to see that this organization that has such an incredible history of making billions of vaccines can also go and make bespoke vaccine one at a time for patients. So I think that's really great.

In terms of timing, it's event driven, so who knows. I mean, we have to wait and see. We have our projections of event rates. But I think the best answer is what we have listed as the protocol completion dates.

Trung Huynh - UBS Limited - Analyst

The investigator said enrollment would be complete by year-end. Do we agree with that?
Eliav Barr - Merck & Co Inc - SVP, Head of Clinical Development & Chief Medical Officer

We haven't discussed that, but I think that the timing is -- I think that, again, enrollment has been going very, very well. I just think that, again, people are so very enthusiastic about this opportunity. If you think about it from a patient point of view, I'm getting a therapy that's directly targeting my cancer. I think that's very cool for them.

Marjorie Green - Merck & Co Inc - SVP, Head of Oncology Clinical Development

We had an investigator a little cranky that they weren't involved in our cutaneous squamous study, and they were really fighting to get as part of that because they're so excited about it.

Peter Dannenbaum - Merck & Co Inc - SVP, IR

Mohit.

Mohit Bansal - Wells Fargo Securities, LLC - Analyst

Thanks for taking my question. Mohit Bansal from Wells Fargo. I have a question related to the Chinese compound. If you go to any of these presentations, I mean, anything related to developmental drugs, you see a lot of new drugs that are not coming from US. I mean, they're coming from China, and you did one of those deals with Kelun, where you could actually get really fast -- you could match up the timelines with the other peers with a fraction of cost.

The question is, number one, are we going to see more of those deals versus deals with US companies in the future because a lot of good science is happening outside of the US? And number two, what do you do to make sure that -- what are the opportunities and pitfalls as well in that approach? Thank you.

Dean Li - Merck & Co Inc - Executive Vice President, President - Merck Research Laboratories

So I'll take that. I mean, the world is large, and the world is contributing to science. The US is pivotal in that, and the US is pivotal not just for US but in training, so many great scientists who are elsewhere. So the world is large, and we are committed to taking the best innovations wherever they are and where we can add value we will do it.

So as you said, we were very impressed with Kelun, and even though when you guys heard the announcement, we had worked with them for some time. So we were very comfortable with them. We're comfortable with the quality of their science, the technology, the way that they do clinical trials, and such. But we're very comfortable with them. And at least for us, that's really important wherever we do business development, whether it be iBio, whether it be Acceleron, whether it be Kelun. This is a critical component part.

But as, you're right, there is great science being done all over the world and especially in China, so we have to look at innovation wherever it occurs, and when it occurs in China, we have to take notice. There is some nuances now especially with certain policies that one has to look straight in the eye and understand what is intended by what is written and also what's the concern behind that. So that one just needs to be a little bit nuanced as we move forward.

But having said it, we will look for important innovation and bring it globally not just to the US wherever we see it. And you've seen it in our recent deal, you've seen it in Kelun, and we will continue to operate that way. But we need to be aware of what's happening in the broader ecosystem and policy.
Hi. This is Dan Ziment here for Terence Flynn and Morgan Stanley. Just two questions. First, your views -- would just be great to hear your views on gastric cancer with the TIGIT combination. We saw data this weekend from another company in the space. I would just be curious how you're thinking about it.

And then on adjuvant lung, from a commercial perspective, you’ve talked about efforts to or where the treatment rates have gone. Could you talk maybe, I know you’ve also discussed diagnosis rates in the early stage, current state of where that is now and where that could go over the next few years? Thanks.

So gastric TIGIT is Marjorie, lung adjuvant is Chirfi and whoever, and I will make a side comment about screening.

We both could answer it, but we divided it up with what we'll talk about.

We're comfortable with where we are with the TIGIT program and the level of investment we've had. We'll see. Gastric cancer is a really tough cancer. It's got both tolerability elements in terms of the patients are quite sick, and it's a relatively resistant tumor.

So I think where -- if you look at what we've been doing, we have a 2870 study in late line to start off with. We've got our Claudin 18.2 ADC. 2870 is reasonably active, so we might bring it a little bit to the front line, and we have to look at whether there's any other opportunities there. It's not an easy cancer. I'm not so sure that TIGIT might be the best place to deal with that particular cancer.

Thank you for the question. I will call on my colleague, Jo, in a moment to take you through a little bit more of how we're thinking about it in the US specifically.

But my broader answer to your question is that we continue to be the absolute leaders in lung. In metastatic, we still have 7 or 8 out of every 10 patients, and that's been stable in terms of market share and we're growing in the early stages of lung both in the US as well as outside of the US. We just received approval in Europe for 671, so we're looking forward to going through the reimbursement process in that region. Japan will come next. So we see continued momentum towards neoadjuvant, adjuvant, or adjuvant post-surgery in the lung setting. So this is really a nice opportunity for us.

Maybe, Jo, you want to talk specifically about the question of diagnosis and treatment rates and so forth in the US?
Joanne Monahan - Merck & Co Inc - SVP, US Oncology

Yes, I'm happy to. Hello, everybody. I'm Jo Monahan, leading the US business for Merck. When it comes to growth in early-stage lung, really, the near-term growth opportunities for us are to continue to drive uptake of KEYNOTE-671 and 091. We're the only one with OS data. We have an NCCN-preferred category recommendation, and we have made very meaningful progress. We're now the market leader when it comes to adjuvant and perioperative combined, even though we came to market third. So that's very exciting. That's an opportunity for continued growth there.

And then continuing to grow the treatment rate of patients who are already diagnosed, we have 65% of them -- we've already almost doubled the treatment rate since we started with KEYNOTE-091. And so I think there's still opportunity to make incremental improvements there.

On the screening side, we are investing in education through the American Cancer Society, through Lung Association. We're doing a lot of work there, but that needle is much harder to move. The lung cancer screening for every 1,000 patients you put into the beginning of the funnel, only a handful of them fall out of the back end of the funnel as far as diagnoses because there's nodule watching and waiting, patients don't go for the follow-up.

So there's the screening rates. It's a risk-based screening. We're based on smoking history and age, and any risk-based recommendation is much harder to implement for providers than age-based recommendations. So I think there's more work we have to do to get better technology to help screening be less invasive, to be more affordable, and to try to get guidelines more broad beyond just smokers for us to make a meaningful impact on the screening side. Doesn't mean we're not still trying, but it is a much harder needle to move and probably a longer-term play for growth than the near-term play.

I don't know, Dean, if you want to add something else.

Dean Li - Merck & Co Inc - Executive Vice President, President - Merck Research Laboratories

I'll just make a cheeky comment. As many of you know, I practice in Utah, and much of my family is from California and some of them are in the medical field. I remind them that their screening rate is seven times less than the state of Kentucky. California and Utah are like at 1% to 2%. Kentucky is much greater. There is a lot of room for improvement.

And I would just emphasize it's really important to talk about lots of screening. There's always debate in terms of breast cancer. When do you do it? 35, 40. Those increments are really important for the breast cancer patient population, but those increments pale in comparison to the fact that the average screening rate in the US is probably in the single digits. So we need to get that right, and I would suggest that all of you call the NIH Director and the CDC and this and say, wow, this is really interesting.

Peter Dannenbaum - Merck & Co Inc - SVP, IR

My understanding is there's no questions from the webcast. So we'll take one more question in the room, and it'll be Daina.

Daina Graybosch - Leerink Partners LLC - Analyst

Thank you for the question. Daina Graybosch, Leerink Partners. In today's discussion, it was notable to me that you haven't demonstrated OS benefit in one of the first adjuvant settings in any of the skin cancer trials. And I wonder, without that OS benefit and advocacy with trials like NADINA, where some physicians would say, let's just wait, you can give IO in metastatic rather than in early. Are you at risk of patients not getting adjuvant therapy in melanoma? And does that put INT at risk in that setting? Thank you.

Dean Li - Merck & Co Inc - Executive Vice President, President - Merck Research Laboratories

What a great question. I think we were talking about it. Eliav?
Eliav Barr - Merck & Co Inc - SVP, Head of Clinical Development & Chief Medical Officer

So let me -- it’s true that we don’t have OS benefit for melanoma, and the reason for that is, in KEYNOTE-054, by the way, this is a good example of why IRA has some issues, we’re still following patients and it’s been years and years. And the reason for that simply is because now patients are dying equally in both arms from cardiovascular disease and Alzheimer and that sort of thing.

And what it actually means is that they’re not dying from cancer. So one of the things that we need to keep in mind is to be able to report out cancer-related deaths. And that’s going to be an important way of doing it. I don’t think it’s going to be an issue though in terms of uptake. It certainly hasn’t been in all but the most cost-sensitive countries.

So I don’t think that this is going to be an issue for INT. Melanoma is such a dreaded disease, and once you’re in metastatic, first-line metastatic, death is feasible in clinical trials as an outcome. And that just shows the much higher risk that patients have, and I don’t think neither physicians nor patients nor policy makers nor frankly payers are going to be willing to let their patient kind of dangle.

Peter Dannenbaum - Merck & Co Inc - SVP, IR

Okay. I want to thank everybody for coming, for your time and attention, and I want Dean to have the last word tonight, but thank you again. Good night.

Dean Li - Merck & Co Inc - Executive Vice President, President - Merck Research Laboratories

So I just wanted to thank all of you for coming. I think what you’ve seen since the transition of the executive leadership in 2021, we’ve made good progress and we’re in good place, and we intend to be in a better place as we continue to move forward and move the programs that you see now, move them forward in the multiple Phase 3, and that we will continue to augment the pipeline along this general strategy that you’ve heard as we move our internal assets more into the visible pipeline and as we also look for continued opportunities to augment the pipeline through business development.

Thank you very much for coming.

Eliav Barr - Merck & Co Inc - SVP, Head of Clinical Development & Chief Medical Officer

Safe travels.