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EDITED TRANSCRIPT

Pfizer Inc To Host Oncology Innovation Day

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PRESENTATION

Francesca M. DeMartino ***Pfizer Inc. - Chief IR Officer & SVP***

Welcome, everyone. Good afternoon, and thank you so much for joining us today, both here at our New York headquarters and online. I'm Francesca DeMartino, Chief Investor Relations Officer for Pfizer, and it is my great honor to kick off a day we've all been waiting for, our Oncology Innovation Day.

Before we get started, I want to remind you that today, we will be making forward-looking statements in discussing certain non-GAAP financial measures. I encourage you to read the disclaimers in our slide presentation, which are also shown on the screen in the room. In addition, the full transcript and video recording of today's event will be posted on the Pfizer IR website, once available, approximately 48 hours post event.

One final note for those in the room, you should have received your unique WiFi access information when you picked up your badge. Please see a member of the IR team with any questions.

We have a robust agenda today, which we've developed to provide you with a comprehensive overview of our new Pfizer Oncology organization. Throughout the afternoon, you'll hear directly from our new Pfizer Oncology leadership team. This team represents top talent from Pfizer and Seagen and is leading our new chapter in the fight against cancer. You'll gain insights into our portfolio, technology, new data and key catalysts and hear why we believe the combination of Pfizer and Seagen is more than the sum of its parts.

To start the day, our Chief Oncology Officer, Chris Boshoff, will unveil the strategic vision for our new Pfizer Oncology organization, followed by presentations on our opportunities in GU and thoracic cancers. Of note, we are pleased to welcome Dr. Tom Powles, a world authority in urothelial cancer, who is joining us to showcase several Pfizer programs focused on UC.

After a short break, the afternoon will continue with presentations on breast cancer, hematology oncology and next-generation approaches to therapy development. We'll end with a commercial outlook.

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You'll note that we have built in 2 Q&A sessions, one before the break and one near the end of the day. We'll have a panel on stage during each session for you to ask your questions related to the preceding presentations. We ask that you please keep your questions relevant to the panelists on stage and related to the presentations you just heard so that we can have the most productive discussion.

The first Q&A session will focus on our oncology strategy, GU and thoracic presentations. The second will focus on our breast, hematology oncology, next-generation and commercial presentations. We'll conclude our event with summary remarks from our Chairman and CEO, Dr. Albert Bourla.

For those attending in person, a reception will follow. Our goal is that you will leave today with an appreciation of the tremendous opportunity we have in Oncology and an understanding of the anticipated catalyst-rich months and years ahead.

Chris Boshoff, who leads our new organization, will be our host for the afternoon. Trained as a medical oncologist, Chris joined Pfizer in 2013 following more than a decade of experience leading academic cancer research. At Pfizer, Chris and his team have delivered numerous cancer medicines from Phase 1 to global approvals, including more than 10 FDA Breakthrough Therapy and European Medicines Agency prime designations.

And now as Chief Oncology Officer, Chris leads end-to-end Oncology R&D and while his background speaks for itself, after 4 months at Pfizer, I can personally attest that Chris is an exceptional leader, a wonderful colleague and friend, and we are really fortunate to have him at the helm.

Joining Chris as speakers today will be several members of his new Pfizer Oncology leadership team: Roger Dansey, our Chief Development Officer; Megan O'Meara, Head of Early Stage Development; Jeff Settleman, our Chief Scientific Officer; Suneet Varma, our Oncology Commercial President; and as I mentioned, Dr. Tom Powles. Chris will introduce our speakers throughout the day, and these leaders will also be joined during the Q&A sessions by additional Oncology leaders and experts.

So with that, let's get started.

(presentation)

Chris Boshoff ***Pfizer Inc. - Executive VP & Chief Oncology Officer***

Welcome, everyone. Welcome. It's a great pleasure to have you all with us here at the Pfizer headquarters. Just over 2 months ago, we actually closed the acquisition of Seagen. And on behalf of the whole leadership team, we're excited now to unveil our new Oncology organization to you today.

Over the next few hours, we'll do a deep dive into our expanded portfolio, our clinical development plans and our capabilities. We will also share more about our strategy, which is assigned and designed to drive significant innovation and growth through 2030 and beyond.

You've heard about a lot now about Pfizer Oncology's renewed focus. As a new organization, we have a bold vision that aligns with Pfizer's purpose. Pfizer's purpose: breakthroughs that drive -- breakthroughs that change patients' lives. Our vision is to accelerate breakthroughs that will help people with cancer globally live better and longer lives.

This drives everything we are doing and reflects our personal mission to improve the lives of people with cancer. Our vision is ambitious, but rightfully so, because as you all know, cancer remains one of the greatest health challenges of our lifetime.

For the first time, 2 million people in the U.S. are expected to be diagnosed with cancer this year. Globally, around 20 million people received a cancer diagnosis in 2022 alone. Approximately 10 million people around the world died from cancer in 2022, and just over 600,000 deaths are expected to occur in the U.S. this year.

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We believe advancing the global fight against cancer will have a tremendous impact on society. And that's why so many companies in this industry are working towards delivering new breakthroughs for people with cancer. In fact, the oncology market is projected to increase to up to $500 billion by 2030.

This year, Pfizer is celebrating our 175th anniversary. We have demonstrated the ability to innovate with urgency, and billions of patients globally have been treated with one of our medicines or vaccines.

Seagen has pioneered the technology and development of antibody drug conjugates, so ADCs, which are emerging as a very, very important tool in the fight against cancer. Over their 25-year history, Seagen developed deep technological expertise to become an industry leader in the ADC field.

And today, nearly half of all the FDA-approved and marketed ADCs use a unique linker payload system developed by Seagen. That's why bringing these 2 companies together has been so exciting for us.

By combining our respective strengths, experience and heritage, we are uniquely positioned to deliver additional breakthrough cancer medicines to more people around the world. As a newly combined organization, our expertise and collective capabilities are now amplified to deliver even more impact for patients than each company could do by itself.

Beginning with expertise. We are bringing together the best from both organizations. We have an exceptionally talented team with extensive experience in oncology.

Innovation. Our pipeline has now expanded significantly. And we are focused on flawless execution, delivering the next generation of breakthroughs.

And lastly, scale. We're poised to have a true global impact. Our new Oncology organization leverages the breadth and depth of Pfizer, including our industry-leading commercial and manufacturing capabilities, to drive broader patient reach.

Before we dive deeper into our future, I would like to briefly touch on what we have been able to achieve over the past decade. Pfizer has been growing Oncology for about 20 years. With the establishment of the first Oncology business unit in 2014, we've emerged from a niche player to a bona fide leader today.

Leading up to 2023, we established a solid foundation with numerous innovative medicines that became new standards of care in several cancers. In fact, our medicines reached just over 2 million patients with cancer last year, which includes our innovative medicines, biosimilars and cancer therapies from Pfizer's hospitals and hospital unit.

We've also seen outstanding revenue growth of our Oncology business over the last decade at a CAGR of over 19%, outpacing the industry average of approximately 10%. With the acquisition of Seagen, we believe our industry-leading portfolio is positioned for strong near-term growth.

We now have 4 additional approved medicines, all of which are first-in-class in their respective indication, and all 4 have demonstrated overall survival benefit. Mid to long term, our early-stage and late-stage development programs have doubled, representing significant future opportunities.

We are at an inflection point of our leadership. We expect to impact many more lives of patients with cancer over the next 5 years plus, aiming to double the number of patients treated with our innovative cancer medicines by 2030.

Leading up to the close of Seagen, we had several months to undertake integration planning and ensure a seamless transition on day 1. The Pfizer Oncology organization, which includes the U.S. Oncology Commercial division and end-to-end global R&D, is designed to improve interaction and collaboration across all functions, from early discovery all the way through to commercialization, facilitating quicker decisions and to accelerate execution.

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Here's our new Oncology leadership team. Any organization is only as good as its people, and I'm pleased to say that we are one of the most experienced and talented groups of oncology leaders in the industry, with nearly 300 years of oncology experience across academia and industry between these leaders combined. These are leaders who've done it before, and they have highly experienced teams working with each of them.

Retention of talent has been critical for us with this integration. And today, we have approximately 50-50 participation of Seagen and Pfizer colleagues in the combined new organization. These colleagues are united around our vision to accelerate breakthroughs for patients with cancer. Our integrated Oncology organization is now fully operational.

To further illustrate the executional excellence of this team, I'd like to highlight 3 examples of how we've rapidly delivered transformational medicines to patients, starting with LORBRENA, which is our third-generation ALK inhibitor for metastatic non-small cell lung cancer. LORBRENA is a small molecule that was discovered by Pfizer scientists using state-of-the-art structure-based drug design. This is a medicine that took less than 5 years in development, significantly shorter than the industry median at the time.

Moving on to ELREXFIO, which is our BCMA-targeted bispecific antibody in development for multiple myeloma. ELREXFIO was first developed by Pfizer scientists, and we significantly accelerated the clinical development time lines. The start of the first pivotal trial, MagnetisMM-3, to ELREXFIO's first FDA approval took less than 2.5 years.

And lastly, moving to PADCEV, which was developed by legacy Seagen scientists in partnership with Astellas. The recent expansion of PADCEV to locally advanced or metastatic urothelial carcinoma was a tremendous feat in speed.

Receipt of the top line report from the groundbreaking EV-302 trial to FDA approval took less than 3 months. And this is a remarkable feat in terms of time lines and a testament to what we believe is PADCEV's groundbreaking clinical value, but also the unbelievable talent of the team that delivered PADCEV to the FDA.

Pfizer is consistently ranked by the Center for Medicinal Research on multiple cycle time metrics using -- and the latest metric from them places us #2 in the industry for oncology. And importantly, across combined legacy Pfizer and legacy Seagen, we have secured 8 FDA approvals for 8 cancer indications in the last 3 years alone.

These examples of rapid execution are great representation of what Pfizer and Seagen were able to achieve as individual companies, but together, we believe our strengths are multiplied. It is also critical to have the resources and scale to deliver these breakthroughs to patients globally.

Pfizer has an extensive global manufacturing footprint with 10 of our sites manufacturing oncology products on 3 continents compared to Seagen's 1 manufacturing site. This robust internal network is critical to ensure agility and responsiveness and puts us in a solid position for growth as our portfolio expands.

In fact, we have 6x the capacity for vial volume for ADC production to what Seagen had alone. We also have 7x more bioreactors for biologics. And we have a supply channel presence in over 100 countries, enabling us to reach large patient populations around the world.

Another example of our amplified impact is through our medical and commercial organizations. We have increased in size and numbers. We have tripled the size of our customer-facing colleagues in the U.S. compared to Seagen alone. And Pfizer has commercial footprint in more than 100 countries compared to 17 for legacy Seagen.

We have cross-trained now our field force, which means we should double our share of voice in key tumor areas. But just increasing size isn't everything. As both Pfizer and Seagen have been building our leadership in oncology for many years, we have each built strong relationships with physicians and customers in our key tumor areas.

Our newly combined presence across both medical and commercial will expand the breadth and depth of our engagement with health

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care providers in both academic and community settings. And lastly, we have the ability to leverage Pfizer's large-scale medical and commercial platforms and capabilities, including our chief marketing offers, to ensure a surround-sound approach with digital channels, analytics and tools.

Let's now move to our strategy. To guide us, we have a new impactful strategy in place. We are focused on 3 main modalities where we have significant depth, world-class capabilities and expertise, small molecules, antibody drug conjugates and bispecific antibodies, including other immuno-oncology biologics. This gives us the ability to combine and adapt modalities to improve outcomes.

For our therapeutic areas, we're building on the cancer types where we have already established presence and where we can further develop our leadership. [These are] across hormonal subtype, genitourinary cancer, including prostate; and urothelial cancer, including bladder cancer; hematology/oncology, including multiple myeloma and certain lymphomas like Hodgkin's disease; and thoracic cancers, which include lung and head and neck cancer.

Within these areas, we're initiating parallel earlier-line trials where the addressable population is the greatest, aiming to both accelerate a new wave of breakthroughs and move approved medicines into earlier lines of treatment. We will continue to also develop targeted therapy opportunities where we believe we can have a true impact, for example, BRAF-positive or HER2-positive colorectal cancer. You will hear much more about our tumor-specific strategies from our speakers today.

Through our strategy, we believe we are positioned to drive transformational global impact through 2030 and beyond. We have the potential to increase the number of blockbuster medicines in our portfolio from 5 today to 8 or more in 2030. We shall provide insight into these 8-plus opportunities today.

With our R&D focus, we anticipate having a tenfold increase in the proportion of revenue from biologics by 2030, presenting potentially more durable revenue opportunity and potentially improved outcomes for patients. These will set the stage for our ambition to double the number of patients treated with our medicines by 2030. We will share further detail of how we plan to achieve these goals through our presentations today.

To close, I'd like to highlight our overall portfolio. As you can see, we have a deep and diverse pipeline, spanning our core modalities and key tumor areas that underpin our strategy. You will hear more about each of these tumor areas and many of these exciting pipeline opportunities during our presentations today.

And with that, we will now transition to our next session on genitourinary cancer, beginning with a reminder of what drives each of us each and every day.

(presentation)

Chris Boshoff ***Pfizer Inc. - Executive VP & Chief Oncology Officer***

Prostate and urothelial cancer are 2 of the most common cancers impacting patients in the United States, both with significant unmet needs. In prostate cancer, close to 300,000 new cases and 35,000 deaths are projected in the U.S. this year alone. And with urothelial cancer, bladder cancer, up to 83,000 new cases are expected this year and 17,000 deaths.

These continues -- there continues to be obviously high unmet need for both types of cancers. In turn, there's a lot of activity in this space, and with many of the industry activity pursuing new treatments for both prostate and bladder cancer.

The prostate cancer market is projected to increase to $26.5 billion by 2030, and the urothelial cancer market is projected to more than triple to $17 billion by 2030. Pfizer has a long heritage in improving outcomes for people living with genitourinary cancers, and we now have an industry-leading portfolio with many exciting opportunities ahead.

Starting with bladder cancer. Our portfolio is anchored with the groundbreaking benefit of PADCEV in patients with locally advanced or metastatic tumors, with opportunities to move to earlier lines of treatment with ongoing Phase 3 studies in muscle-invasive bladder

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cancer.

In metastatic disease, we are developing a novel HER2-directed ADC, disitamab vedotin, which has shown very promising early clinical data. The ongoing pivotal program is evaluating disitamab vedotin in the subset of patients with HER2-positive disease, both high expressers and low expressers, with planned registrations in second line as monotherapy and in first line combined with pembrolizumab.

Finally, in nonmuscle-invasive bladder cancer, we are evaluating the combination of sasanlimab, our subcutaneously administered PD-1 antibody, with BCG to improve outcomes for patients with high-risk nonmuscle-invasive bladder cancer. To share more about this portfolio I'd now like to introduce 2 of our speakers for this session.

First, I'd like to formally introduce Roger Dansey, who is our Chief Development Officer. Roger joins us from Seagen, where he was President of Research and Development. Previously, Roger was therapeutic area head of late-stage oncology at Merck, prior to that, clinical development leadership at Gilead and Amgen.

Roger holds an MD from the University of the Witwatersrand in Johannesburg, South Africa. And he brings unmatched oncology clinical drug development experience to Pfizer as well as the industry gold standard for executional excellence.

And then I'd also like to welcome Dr. Thomas Powles, who is professor of genitourinary oncology at the University of London and Barts Cancer Center. Dr. Powles is the Head Investigator for the PADCEV EV-302 trial and a world-renowned urological oncologist. We're happy to have him here today to share his perspectives on the exciting data from PADCEV and bladder cancer as well as additional medicines we have in development for bladder cancer.

I'll now turn it over to Dr. Powles. Thank you.

Thomas Powles ***University of London and Barts Cancer Centre - Professor of Genitourinary Oncology***

Thanks, Chris. It's really kind of you. Thank you for inviting me, and it's nice to see you. Chris asked me to come today, and I jumped at the chance. I live in London. You can see by my accent, probably. And the reason I came was because I think we are at a pivotal moment in oncology. We've not been at a point like this for some period of time.

I was involved in the immuno-oncology transformation and partly involved in the targeted therapy transformation. And I think we're going through one of those transformations at the moment, and I wanted to describe what my views are of those. I'm very lucky in that respect.

I've led 23 big randomized trials in my life. Some have been successful, most have not. But I'm going to describe today the one that has been most successful, which was presented recently at ESMO. PADCEV, enfortumab vedotin, is what I call it, is an antibody-drug conjugate. It targets Nectin-4. Nectin-4 is expressed on almost all urothelial cancers. And patients with advanced urothelial cancer have a really poor outcome, meaning survival of about a year historically.

PADCEV, it binds to the system. It's internalized rapidly. It is then degraded by the lysosome. And from there, MMAE, the microtubule disrupting agent, is activated. And at that point, it triggers apoptosis. It also causes cell cycle arrest through the endoplasmic reticulum. There's the immunogenic cell death also. So that's the second mechanism. And thirdly, it's important to recognize that MMAE is permeable and can cross the barrier into other cells and trigger another apoptotic process.

The drug itself, therefore, is a really attractive target for urothelial cancer, but potentially other cancers also. This is the study which I led, and I think it was -- at the time we designed it, we felt it was ambitious. It turned out that, that wasn't the case. We were right to be ambitious.

When we designed it, we knew that enfortumab vedotin was associated with responses in patients who are heavily pretreated. We know that -- well, I felt it was probably the most active single agent that we had, but you might be aware that we've struggled to combine drugs with immune checkpoint inhibitors in urothelial cancers previously.

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So we did Phase 2 work, and that Phase 2 work showed response rates in advanced disease of 70%. That was a little bit unprecedented in urothelial cancer, who are used to about 40%, but Phase 2 data can be misleading. And so it was important to do this large randomized Phase 3 study.

The randomized Phase 3 is a classic 850-patient, first-line metastatic urothelial cancer, enfortumab vedotin, PADCEV plus pembrolizumab, KEYTRUDA, the 2 drugs together versus standard chemotherapy. During the conduct of the trial, the control arm changed the -- we allowed the introduction of avalumab. 31% of patients got avalumab in the control arm. That's actually quite a high proportion of patients.

The endpoints, dual endpoints, progression-free survival and overall survival with some secondary endpoints around safety and response. You can see from here, these are the primary endpoints of progression-free and overall survival. And they are overwhelmingly positive, with a 45% reduction in the risk of progression or death, and a 53% reduction in the risk of death.

These are, by far, the most impressive data we've ever seen in urothelial cancer. In fact, it's the first time we've beaten frontline chemotherapy, gem/cis or gem/carbo, in urothelial cancer. And to beat it by 53%, the reduction of risk of death of that proportion was unprecedented.

The control arm actually performed really well in this study. Historically, as I said, the median survival going back in other trials like DANUBE was more like 12 to 14 months. So this really was exceptional data. It's also worthwhile noting the CR rate, complete response rate, was 30%. We've never seen anything like that before. And that's why we're so excited about moving this into the perioptic setting.

It's important to also recognize that in this study, we enrolled all comers. We enrolled patients, irrespective of their PD-L1 status, cisplatin eligibility, which I think will become a thing of the past. But we've got very obsessed in urothelial cancer with whether a patient has cisplatin or carboplatin. It's my feeling that the drugs have more similarities than differences. Other people disagree with me on that issue.

But this was an all-comer study for the entire population. And it's likely because of these results -- historically, not all patients have been offered chemotherapy in urothelial cancer. The outcomes have been modest. It's quite toxic. I suspect the pie will increase. I think more people will be offered EV-pembro that were previously being offered platinum-based chemotherapy.

Adverse events are really important part of everything that we do. They're super important for patients, too. EV-pembro was given until progression, platinum-based chemotherapy given for 6 cycles. You can see here, actually, the grade 3 or 4 adverse events were less frequent for EV-pembro than for platinum-based chemotherapy, 70% versus 56%.

My experience with platinum-based chemotherapy and of my colleagues is not fantastic. It's associated with quite bad renal toxicity. In fact, if it was developed tomorrow, it probably wouldn't get off the ground because you've got to give IV fluid beforehand for 4 hours, then you get the platinum. We have developed 3 antiemetic drugs to control the nausea and neutropenic sepsis.

I've got a patient at the moment in our hospital who's on their third cycle. The cancer is growing, the neutrophil count is 0.1. They've got infection, they're on IV antibiotics. It's a complicated regime to give. Unfortunately, the dose is different from that. It is associated with adverse events. Skin toxicity in the first 3 or 4 cycles and peripheral neuropathy, which increases at cycle 6 to 12.

My experience, my personal experience of this, and I'd spend a lot of time speaking to people in rooms not dissimilar to this about adverse events of drugs is that it's manageable. In fact, I think it's easier to give them platinum-based chemotherapy. I think dose delays and interruptions are required.

An early recognition of new toxicity is really important. When we go to med school and oncology school, we're taught for years about adverse events of chemotherapy. And then when new drugs arrive, we're supposed to just pick them up immediately. I think we need to think more carefully about that. But I think this is a total regime. I think it's going to be very widely used throughout the world.

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The data made a huge splash at ESMO. I was lucky to present it. I made less of a splash. The data was amazing and spoke for itself. We got 2 standing ovations, which is a rather unusual thing and made me quite anxious at the time. Why did it make such a big splash? It made such a big splash because we've never seen something like this before.

Unlike pancreatic cancer, I think when we beat gemcitabine in pancreatic cancer, it will be a similar moment. It's taken such a long time and has been so frustrating to see these patients come, struggle and then die of their disease.

That's just the first part of the story because the story in urothelial cancer is going to continue. And I got a feeling the story might get better. We really need to cure more of these patients. We don't yet know about some of the durability issues of EV-pembro. I think the median overall survival will turn out to be about 3 years, at 36 months. There's a bit of instability in that curve.

But the CR rate of 30% is really intriguing. I have treated maybe 20 or 30 patients with the combination. And we have patients who we've given 4 or 5 cycles, too, some 8 or 9, and they've got into durable remissions. And we stopped some of the drugs in some of those patients, and the cancer's not come back.

If we give these drugs to patients at the time of their operation when half of them are cured with cystectomy alone, with or without adjuvant nivolumab, I think we might be able to increase the cure rate further. And I think we might be able to cure of some of these patients with systemic therapy alone.

And I hope it's going to be 30%, 40%, dare I say it, 50%. I don't know what's going to happen. But I'm very excited about these 2 trials, one in cisplatin eligible, one in cisplatin ineligible. One of them is enrolling, one of 'em completed enrolling. You can see here the date of '26 and '27 when they're expected, but we'll probably get some interim analysis results potentially before then.

Disitamab vedotin is a drug which I'm also excited about. I've got personal experience with this drug as well. We've treated about 20 patients. And I can tell you, it's also a very active antibody-drug conjugate. Disitamab vedotin has a mechanism of action which is -- it's targeting HER2. It's distinct from some of the other HER2-targeted therapies. It's actually internalized more quickly than trastuzumab. And the reason for that is it binds to a different epitope.

It also has MMAE as a payload. So the mechanism of action in terms of the microtubule disruption, the immune component and potentially a good partner with immune therapy, but also the bystander effect obviously applies as well. And there's a table there looking at other HER-targeted therapies and how this may compare.

This drug is approved actually in China, and it's used in gastric cancer, and it's also used in urothelial cancer. As I said, it's a HER2-targeted therapy. It looks like that there is some enrichment in those patients who heavily overexpress the biomarker. But you can see actually here, the vast majority of patients have expressed HER2. And on top of that, the response rate is about 50% in heavily treated urothelial cancer.

Now remember that enfortumab vedotin dosing was 40%. So now I'm not a great one for comparing Phase 2 studies, but I'll just say that this drug is active. We've given it to our patients. It's active. The adverse event profile, because it's targeting HER2 and not Nectin-4, is a distinct toxicity profile, perhaps less skin toxicity, in my opinion.

The high rate of durable responses that we've seen with monotherapy is actually increased again when we combine it with an immune checkpoint inhibitor. This is toripalimab, not pembrolizumab. This is Chinese data again. And you can see here both from the waterfall plot and the spider plot that there will be deep durable responses.

I think the point that I'd kind of like to make is that I'm not convinced that all partnerships with ADCs and immune checkpoint inhibitors is going to be synergistic or additive. But it looks like MMAE may be a good partner, a good payload partner. We saw that in EV-302. We may be seeing that with disitamab vedotin also. As you can imagine, there's an ambitious plan for disitamab vedotin.

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Chris (inaudible) which I was -- which I'm bought into.

I'm also bought into the strategy for this agent. As a single agent, it has an accelerated approval with -- sorry, has breakthrough status with the FDA. But it's also being explored in a Phase 2 study to confirm that monotherapy activity. Our site is taking part in that study at the moment. And we're enjoying using the drugs, and we're seeing deep responses, as I said.

It's also being explored in a frontline randomized Phase 3, a trial design not dissimilar to the EV-pembro trial, which I just previously showed you. (inaudible) developed subcutaneously, which is different from the other immune checkpoint inhibitors, which have been developed intravenously. Although some have data or more data subcutaneously. It's a potent PD-1 inhibitor. It has high receptor affinity, and it's a drug which is being explored in nonmuscle-invasive urothelial cancer.

I described advanced disease, and I talked about enfortumab vedotin and pembrolizumab and disitamab vedotin. I talked about that muscle-invasive setting, where we do the cystectomy to cure patients. And we hope that by giving EV-pembro neoadjuvantly, we're going to cure a significant proportion of patients.

And now earlier in the disease, nonmuscle-invasive urothelial cancer, where patients normally just have cystoscopy to scrape away their cancer, the standard treatment for 40, 50 years, perhaps longer, it's actually been BCG therapy. It's an immune therapy. No one knows exactly how it works, which I think is intriguing. But if you go on PubMed, you'll find 100 different ways in which it may work.

But you also know that in this nonmuscle-invasive space, pembrolizumab currently has a license. But in those patients whose cancers have progressed after BCG, this is a more ambitious plan than that. This is to go earlier in this high-risk population. BCG is the control arm. BCG is given as an initial therapy and a maintenance therapy for a period of time. You'll be aware there's a BCG shortage from a global perspective.

In this study, it's 3 arms: it's BCG plus sasanlimab, BCG plus sasanlimab but no maintenance period of the BCG and then BCG alone. I think this is an exciting study. We're hoping to see the study readout in the not-too-distant future. It's an ambitious plan. And as Chris described earlier, the Pfizer Group has a very ambitious strategy.

I'm now going to turn it over to Roger to do prostate cancer. Thank you very much for your attention.

Roger Dansey ***Pfizer Inc. - Chief Development Officer, Pfizer Oncology***

Okay. Good afternoon, everyone. It's great to be here. And I would like to just reiterate what Chris said from a sort of an ex-Seagen side. I'm extremely excited. I mean, we have 2 organizations that already are a level of high excellence. We've brought them together. This idea of best of both is extremely appealing.

And more importantly than anything else is the portfolio is really, really meaningful in terms of what we can potentially do to help people. That's our North Star. That's our driving force in terms of why we do this every day is to make a difference in patients' lives. And certainly, for me, it's very exciting to see all of these programs, great science with good people. Hopefully, we'll bring forward some great medicines.

So turning our attention to prostate cancer, which really can be broadly divided into castration-resistant and castration-sensitive disease with actually large addressable populations across this continuum of disease. Our portfolio is anchored by XTANDI. It's the only antigen receptor-signaling inhibitor, which is actually approved across the prostate cancer continuum.

As we seek to further improve outcomes for men with prostate cancer, we are building on that foundational drug, XTANDI, with the next generation of combinations. We have 2 novel combination approaches: TALZENNA, which is our PARP inhibitor; and mevrometostat, our EZH2 inhibitor, both of which are being combined in development trials with XTANDI. And these 2 will be the focus of my presentation.

However, before we get that, I'd like to remind you just what an advancement XTANDI by itself has been in prostate cancer. I think you can appreciate when you look at the weighted evidence on the slide and demonstrated by all the graphs showing improvement in

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progression or metastasis-free survival in all disease states.

To emphasize how meaningful this therapy has been and sort of analogous to Tom talking about the impact and the size of the treatment effect with PADCEV and KEYTRUDA, control of disease progression varies from 60% to 80%. And in addition, the gold standard outcome, which is overall survival, there's an overall survival benefit in every disease state where mature results are available. It's really quite remarkable.

And actually, as recently as November of last year, XTANDI gained approval in a new population, which is represented by the results of the EMBARK trial on the far right of the slide. XTANDI now offers a new option for men with nonmetastatic castration-sensitive prostate cancer with biochemical recurrence at high risk for metastases.

Moving now to TALZENNA. TALZENNA is building on the XTANDI backbone by targeting inhibition of PARP, a pathway that synergizes with antigen receptor inhibition. Approximately 30% of men with prostate cancer harbor alterations in homologous recombination repair genes, and these alterations are particularly sensitive to inhibition of PARP.

In addition, patients whose tumors harbor a gene alteration, the HRR type, generally have an inferior prognosis compared to those who do not. And so this group of patients represents a truly high unmet need, both in castration-resistant and castration-sensitive disease. Results of the Phase 3 trial of TALZENNA, in combination with XTANDI and the TALAPRO 2 trial, have led to global approvals.

And TALZENNA is now indicated in the United States for men with HRR gene alterations and in the European Union for all patients with metastatic CRPC. We await the results of the final survival data midyear, that's this coming midyear '24, at which time we will evaluate whether these results could be used to support additional regulatory filings for this combination.

Moving now to TALAPRO 3. TALAPRO 3 is evaluating the benefit of TALZENNA plus XTANDI for patients with HRR gene alterations in this earlier treatment setting, metastatic CSPC. This trial has actually completed enrollment, and we expect the first data readout in the second half of 2025. If positive, this combination has the potential to meaningfully prolong progression-free survival, which should lead to extended treatment duration compared to the metastatic castration-resistant setting.

Moving on now to mevrometostat, which is our EZH2 inhibitor. EZH2 plays an important role in controlling gene activity and is often associated with prostate cancer cell proliferation. Mevrometostat in combination with XTANDI has demonstrated promising synergy in preclinical (inaudible) as you can see on the slide. And this promising preclinical data supported the initiation of a trial evaluating mevrometostat and XTANDI in heavily pretreated patients with metastatic CRPC.

And we believe that this molecule is potentially the first EZH2 inhibitor to be -- has the potential to be approved in prostate cancer, obviously subject to the trials being positive. The updated results of the dose-escalation portion of the Phase I study are shown here. And the combination of mevrometostat plus XTANDI has delivered a meaningful prolongation of radiographic progression-free survival in patients who have already failed XTANDI or abiraterone treatments.

For the post-XTANDI patients, and a radiographic PFS of 11.7 months was achieved, and you can see that on the right side of the table. And this benefit is even more pronounced in patients who have only received prior abiraterone, with a median radiographic PFS of 17.1 months.

Both of these results are extremely encouraging as the median rPFS for patients who previously received either XTANDI or abiraterone and treated with available therapies is only 5 months. Of note, the most common treatment-related AEs in the study were diarrhea, dysgeusia and anemia.

Based on the strong signal, we are planning to initiate 2 pivotal studies in metastatic CRPC later this year. The first Phase 3 will evaluate mevrometostat plus XTANDI compared to either XTANDI or docetaxel in patients who previously received abiraterone.

In parallel, and that's on the right side of the slide, we are planning to start a second Phase 3 study, which will compare mevrometostat

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plus XTANDI versus a placebo-based with XTANDI, and this is in patients who are treatment-naive with metastatic CRPC. So bringing the entire genitourinary cancer program together, and as you've heard from the presentation from Chris, from Tom and from myself, we are really excited by the opportunity for Pfizer Oncology in GU cancer.

In the near term, we have these 2 Phase 3 trial starts with mevrometostat, which I've just walked through with you. We also expect near-term data readouts for TALZENNA and XTANDI with that final OS data later in the year. The trial that Tom ran through on sasanlimab with nonmuscle-invasive bladder cancer combined with BCG, a really exciting trial, that's a proximal readout. And disitamab vedotin, our other approach to bring a vedotin-based ADC to bladder cancer in second-line HER2-positive and HER2 low urothelial cancer, metastatic urothelial cancer.

So we have a lot of near-term data readouts, which I think are pretty exciting, potentially very exciting. Longer term, obviously, we'll have numerous readouts from registration trials. And again, I think as Tom emphasized, the PADCEV and KEYTRUDA story has not stopped.

There's the top line muscle-invasive bladder cancer data, which will be available potentially as early as next year. And this has tremendous potential, just based on PADCEV and KEYTRUDA's track record, both of these highly active agents. There's a strong possibility these trials will be positive and with the potential for this combination to really become the new standard of care in a large patient population.

In addition, we anticipate the readout of disitamab vedotin plus KEYTRUDA in that frontline metastatic HER2-positive urothelial cancer as well as the pivotal trials of mevrometostat plus XTANDI in metastatic CRPC. So with our innovative portfolio across prostate and urothelial cancers, GU has the potential to emerge as the largest growth driver among our tumor areas of focus. And I believe we're well positioned to reach a significant portion of the over 150,000 addressable patients in the U.S. in the next decade.

Thank you, and I'll turn this back to Chris to continue with our tumor area presentations.

(presentation)

Chris Boshoff ***Pfizer Inc. - Executive VP & Chief Oncology Officer***

Thank you. In thoracic cancers, we're advancing portfolio across both lung cancer and head and neck cancer as well as lung -- as you all know, lung cancer is the #1 cause of cancer deaths globally. There were approximately 280,000 new cases of lung cancer in 2023 with approximately 130,000 deaths. Head and neck cancer occur in the larynx, throat, lips, mouth, nose and salivary glands.

In 2023, approximately 67,000 new cases of head and neck cancer were diagnosed in the U.S., and there were approximately 15,000 deaths. There's a high, very high unmet need for new options for curative intent or to prolong survival. The lung market is very active today and projected to increase to $45 billion by 2030 and the head and neck cancer market to $3 billion by 2030.

I'm now pleased to introduce Dr. Megan O'Meara, who is our Head of Early Clinical Development. Megan joins us from Seagen, which she joined in 2011, and most recently was Head of Clinical Development at Seagen. She's a board-certified medical oncologist.

Megan received her MD from the University of Arizona and then internal medicine residency at the University of Washington. She completed her medical oncology fellowship at the Fred Hutchinson Cancer Institute in Seattle and also completed the postdoctoral fellowship at the University of Washington. Thank you, Megan.

Megan O'Meara ***Pfizer Inc. - Head of Early-Stage Development, Pfizer Oncology***

Thanks, Chris. Good afternoon, and thanks, everybody, for joining today. I can tell you, I'm thrilled to be here and really excited to tell you more about how we are developing potentially best-in-class medicines for thoracic cancers, including lung cancer and head and neck cancer.

So as Chris touched on earlier, and you can see here, our combined pipeline provides very broad opportunities for development in the thoracic space, including, but not limited to, the 11 medicines shown here. This robust lung and head and neck portfolio spans Pfizer

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Oncology's core scientific modalities, with clinical stage assets across small molecules, ADCs and immuno-oncology biologics, which also includes bispecifics.

On the left, you can see our small molecule programs. This includes our SHP2 inhibitor and our oral STING agonist, which are both in Phase 1. And then you can see below our approved medicines, including our third-generation ALK inhibitor LORBRENA and combination therapy, BRAFTOVI and MEKTOVI, which was recently approved for adults with metastatic BRAF-mutant nonsmall cell lung cancer.

In the middle are our innovative ADC programs. This includes B6A, which is an integrin beta-6-directed ADC that was recently assigned the nonproprietary name sigvotatug vedotin. And it recently began a Phase 3 study in second to third-line nonsmall cell lung cancer.

Then below that, we also have some other Phase I ADCs, one directed at PD-L1 with a vedotin payload, also a CEACAM5 with a topo payload. And then finally, on the right, you can see our immuno-oncology biologics. This includes a novel EGFR-targeted bispecific that's just entered the clinic.

So today, what I'm going to focus on is the progress we've made with LORBRENA as well as our vedotin ADCs directed at integrin beta-6 and PD-L1. So first, to set the stage, I'd like to share a little bit about the epidemiology of nonsmall cell lung cancer.

As you can see on the left, there are groups of patients with actionable genomic alterations such as the ALK gene. Each patient's cancer is unique. And so testing for specific genomic alterations may allow for more personalized treatment. Treatments can also differ based on histologic subtypes.

As shown on the right, nearly 3/4 of the disease is nonsquamous and about 1/4 of squamous. As a pioneering leader in precision medicine, we've developed several targeted lung cancer therapies, including XALKORI, which was the first precision medicine in lung cancer targeting the ALK gene. And more recently with LORBRENA, our third-generation ALK inhibitor, which is emerging as the potential standard of care for ALK-positive nonsmall cell lung cancer. I'll talk more about this shortly.

And then looking ahead, you can think about our innovative pipeline of potential first-in-class therapies, which looks to maximize our opportunity in lung cancer across broader populations using a variety of innovative modalities, including novel ADCs and new targets. So I look forward to sharing an example of this related to an ADC directed to integrin beta-6, which is a target expressed on large majority of lung cancer.

Shortly following development of XALKORI, our expert Pfizer medicinal chemists embarked on further addressing unmet need in ALK-positive nonsmall cell lung cancer with LORBRENA. With the unique macrocyclic structure unlike any other TKI -- ALK TKI, it was designed to intentionally overcome ALK resistance mechanisms and also better address brain penetrants.

Of note, brain metastases are particularly common in ALK-positive nonsmall cell lung cancer. And so I'll touch more on the importance of this shortly. As you can see on the table on the right, the green shading demonstrates the broad mutational coverage of LORBRENA against some of the most common tumor mutations that drive resistance to other ALK inhibitors. This shows LORBRENA's unique potential to differentiate in this space.

And then I also want to point out, as Chris talked about earlier, that we were able to rapidly execute the development program for this medicine, leading to approval in less than 5 years after IND submission. So through the Phase 3 CROWN trial investigating lorlatinib versus crizotinib, we are able to validate the rational chemistry design in the clinic. The FDA approval of LORBRENA is in the frontline setting for ALK-positive nonsmall cell lung cancer is based on these compelling results from the trial.

As you can see here, LORBRENA demonstrated a significant class-leading 72% reduction in the risk of progression or death compared to our original molecule crizotinib.

Not only is this improvement in the outcome compared to crizotinib quite remarkable, but as you can see, the tail of the curve has plateaued, suggesting that patients could remain on treatment for a long time before they go on to progress.

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So as I mentioned earlier, LORBRENA was designed to better address brain penetrants. Importantly, upon initial diagnosis, up to 40% of ALK-positive non-small cell lung cancer patients will be impacted by brain metastases.

As you can see on the left, LORBRENA demonstrated meaningful improvement in the reduction of brain metastatic progression in the CROWN study with a hazard ratio of 0.08. This is rarely seen.

And as you noticed on the right, reduction in risk of brain mets has impact across patients with or without brain mets at baseline. In fact, if you look at the far right, at the time of this analysis, only 1 subject of the 112 without brain mets at baseline went on to develop brain mets on the low brain arm of the study, suggesting a protective effect.

Now as shown here, there have been several Phase 3 studies in ALK-positive non-small cell lung cancer that carry crizotinib control arms. Head-to-head comparisons cannot be made, but I'd like to point out that the crizotinib control arm in all 3 of the trials shown here performed similarly.

Now if you look at the experimental arms, lorlatinib appears to have performed best. As you can see on the left, the 3-year follow-up data from the CROWN study show that LORBRENA demonstrated a 73% reduction in risk of progression or death compared to crizotinib, corresponding to a hazard ratio of 0.27.

Importantly, the curve is still plateaued, and we've not yet reached median PFS or overall survival. Median duration on treatment for LORBRENA was 33.3 months at a time of this analysis with 61% of patients still receiving LORBRENA versus 8% on the crizotinib control arm.

So in summary, these remarkable results support LORBRENA as the potential standard of care in ALK-positive non-small cell lung cancer. So now what we're doing is gathering the 5-year CROWN data, and we look forward to presenting what could be potentially unprecedented results at an upcoming medical conference.

Okay. So switching gears. Now I want to touch on our growing portfolio of innovative ADCs that have the potential to improve the lives of many patients living with thoracic cancers, including lung cancer. Sigvotatug vedotin is an integrin beta-6 directed ADC, also known as B6A. Integrin beta-6 is highly expressed across a variety of solid tumors and is typically associated with a poor prognosis.

In non-small cell lung cancer, integrin beta-6 is actually expressed on greater than 90% of tumors. So you can see here on the right, immunohistochemistry staining examples of integrin beta-6 across histological subtypes.

In fact, other groups have tried to target integrins for cancer therapies, but they've been limited by challenges with normal tissue target expression. Our team of researchers intentionally designed this integrin beta-6 antibody for high target selectivity, limiting binding to other integrins that are more likely to be expressed in normal tissues, potentially reducing off-target toxicity.

And then in addition, just thinking about what Dr. Powles referenced this morning with the mechanism, by pairing this target with the vedotin payload, the MMAE release leads to not only direct cytotoxicity and bystander effect but also immunogenic cell death, leading to potentially complementary activity with immune checkpoint inhibitors like anti-PD-1s.

So today, I'm pleased to show you some encouraging new data from our Phase I study of sigvotatug vedotin. This is a heavily pretreated Phase 1 population of non-small cell lung cancer patients with limited standard of care options and high unmet need.

For example, just to put it in context with docetaxel therapy, one would expect a response rate in the low teens. These data are in a subset of non-squamous non-small cell lung cancer patients across active dose regimens of 1.25 milligrams per kilogram or higher.

If you look on the left, you can see the waterfall plot. If you look at this inflection point, nearly 2/3 of patients are showing tumor regression. In this Phase I study, the overall response rate with the selected Phase 3 dose of 1.8 milligrams per kilogram biweekly, which

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was supported by regulatory authorities, was over 30%, 31.3% to be exact.

And then if you look here on the right, you can see the spider plot within this cohort. And you can see many patients had deep and durable responses with some on treatment more than 18 months. And so we're continuing to follow the data, and we're looking forward to sharing more updated data at an upcoming medical conference later this year, including survival follow up.

And then now here, this is our design for our sigvotatug vedotin pivotal trial, which is now up and running. We designed this trial specifically based on the learnings from our Phase I data. And you saw from the previous slide that in this data set, we saw the best clinical activity in the non-squamous subset.

Now as I noted in my upfront slides, nearly 3/4 of patients with non-small cell lung cancer have non-squamous disease. So given the favorable activities observed in the subset from our Phase I, we'll be focusing on second to third line taxane naive non-squamous non-small cell lung cancer.

Patients will be randomized to sigvotatug vedotin or docetaxel, and the primary endpoints of the study are objective response rates and overall survival. And I'm pleased to say the study is now recruiting. It's up and running, and we anticipate a readout in 2026 or 2027.

So let's move on to head and neck cancer now, where there's also a substantial unmet medical need. We see significant opportunity to improve upon the standard of care, particularly in patients with unresectable disease in the locally advanced or metastatic setting, which you can see here in the pie chart for the 3 lighter blue colors accounts for approximately 60% of patients with head and neck cancer.

We have many innovative programs that we believe can make a difference for people living with head and neck cancer, and I'm going to focus on one of them today, our PD-L1 targeting ADC. So shown here is our first-in-class PD-L1 targeting vedotin ADC.

It's interesting, prior to initiating this program, we considered the target to be interesting for multiple diseases just given the high expression of PD-L1 on tumor cells. And given this, we've questioned, why haven't others come up with PD-L1 directed ADCs.

And then in the lab, when we conjugated our vedotin drug linker to commercially available PD-L1 antibodies, they actually didn't work well as ADCs. They don't really internalize.

And so our talented team intentionally created a PD-L1-directed ADC with excellent internalization. So as shown on the right, when we compared the extent of internalization to other PD-L1 backbones, including atezolizumab, avelumab or durvalumab, our antibody achieves much better and much faster internalization.

And in addition, we've been able to demonstrate preclinical activity across the PD-L1 spectrum even in PD-L1 low-expressing tumors. So looking ahead, again, we see opportunities to leverage this vedotin immunogenic cell death mechanism and also explore potential combinations with immune checkpoint inhibitors with this ADC.

So here, I'm excited to show you what is the first disclosure of clinical data from our Phase I study, which is demonstrating interesting initial efficacy. So if you look on the left, you see the data from the head and neck subjects in dose escalation greater than or equal to 1.25 milligrams per kilogram.

At the inflection point of the waterfall plot, approximately 2/3 of patients are showing some tumor regression with a confirmed objective response rate of 21% and an unconfirmed objective response rate of 50%. We continue to follow this data closely.

And to put it in context, again, these are very heavily pretreated patients with limited options. In this particular data set, the patients here received a median of 4 prior lines of therapy and all of the patients' tumors have previously progressed on immune checkpoint blockade. So in this setting, to put it in context, one would expect single-digit response rates with available therapies.

And then you can look on the right and you can see the spider plot, which shows ongoing responses, including patients currently

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approaching 8 to 9 months on treatment. So this is early data. We plan to present additional data at an upcoming medical conference later this year. We also plan to initiate PD-1 combo studies in the frontline setting as part of the Phase 1 trial.

So I've been excited today to share some data from 2 promising ADCs and our thoracic pipeline, one targeting intergrin beta6 and the other targeting PD-L1. We've generated consistent preclinical data sets supporting that vedotin drives immunogenic cell death, and we see potential clinical synergy with anti-PD-1.

So as you can see here, enhanced clinical benefit has been seen across multiple combination studies exploring vedotin ADCs with anti-PD-1s. And that includes with the recent EV-302 pivotal data in urothelial cancer with PADCEV and KEYTRUDA that was just presented by Dr. Powles.

So we're making nice progress advancing these efforts with PD-1 combos ongoing for sigvotatug vedotin and planned for the PD-L1 ADC in the Phase 1. And so this will help us drive development into earlier lines of therapy.

So given unmet need across thoracic malignancies worldwide, Pfizer is committed to developing the next generation of potential breakthroughs in this space. Today, I was able to show you a significantly expanded thoracic portfolio with encouraging data for LORBRENA, sigvotatug vedotin and our PD-L1 ADC.

Now looking ahead, we're excited about the potential catalysts shown here. In the near term, this includes that -- we've actually just initiated enrollment of our Phase 3 study exploring sigvotatug vedotin in second to third line non-small cell lung cancer. Soon, we'll be sharing our 5-year data from the LORBRENA CROWN study. And then we have the evaluation of data-driven opportunities for our PD-L1 ADC in PD-L1 expressing tumor types, including head and neck cancer.

And then looking out even longer term, we're looking forward to broader opportunities in the thoracic space with initiation of a Phase 3 study exploring sigvotatug vedotin in frontline non-small cell lung cancer. And then looking a little further out, we're very excited about data readouts from the Phase 3 study ongoing of sigvotatug vedotin in second to third line non-small cell lung cancer and the planned first-line lung cancer -- non-small cell lung cancer study.

So putting this all together, Pfizer is well positioned to bring this innovative pipeline of potential breakthroughs to a significant proportion of the over 150,000 total addressable head and neck and lung cancer patients in the U.S. across the disease continuum in the next decade.

Thank you. Now I'll turn it over to Chris for Q&A.

QUESTIONS AND ANSWERS

Chris Boshoff ***Pfizer Inc. - Executive VP & Chief Oncology Officer***

Thank you Megan, who will remain on stage and we'll be joined by the other presenters as well, and then we'll have a Q&A session for all of you. If you'd like to ask a question in the room, please line up at one of the two standing microphones located on either side -- and please introduce yourself before asking your question. For those online, please submit questions through the streaming platform, and, if time permits, we'll address those questions as well. We ask that you reserve specific commercial questions for next session -- our next Q&A session. We will also be joined by Suneet Varma, our Commercial President.

In addition to our speakers, I'd like to introduce Dana Kennedy, our therapeutic area development head for genitourinary cancer. And Dana has an interesting career. Dana was at Seagen then came to Pfizer for nearly 10 years and now lives in Seattle now. Yes, still with us. Thank you.

Okay. So we'll start on this side on the left.

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Trung Chuong Huynh ***UBS Investment Bank, Research Division - Analyst***

Trung from UBS. Professor Powles, I have one for you, and I've got another prostate cancer one if that's okay. So for Professor Powles, the EV-302 study is getting regulatory review in the EMA at the moment. I'm just wondering your thoughts on just the appetite for European regulator -- sorry European payers, I guess, with the 15-month benefit and how we've seen paradigm shifting products before enter but having trouble with payers. So just not commercial, but just the need that the 15 months is that the real unmet need there?

Thomas Powles ***University of London and Barts Cancer Centre - Professor of Genitourinary Oncology***

I can answer that, and I'm not involved in any of the processes associated with NICE or the EMA, if I can speak very frankly, and I don't know anything that you don't know. The -- I think the key to this is that when your cost for quality, which is really important for reimbursement, I know it's not important for EMA approval although some people are always suspicious that cost is in the back of the EMA's mind, and I won't comment on that.

But when you get the previous overall survival of 1 year and you double that, and you get a whole year of additional life, that makes the cost per quality analysis actually a lot more favorable. When we have progression-free survival advantage without OS, which often do get approved but don't get reimbursed, that's because when you look at the cost per quality, the 1 year of life is really hard to extrapolate from those PFS curves.

When you have those curves that go so far apart and stay apart, I think the reality will be that, that cost per quality will be relatively acceptable. And when you think about it, organizations like NICE and Spanish organizations and the Italian organizations, when you think about sort of 70,000 per cost per quality when you're actually saying, okay, we're gaining at least a year, maybe even more than that with this, those numbers then become realistic.

Now in terms of how you negotiate the price with MSD and the -- I'm not involved in that. What I can tell you is 2 things. Number one, when transformative data does come along even to the U.K., and I know a little bit about that, when we see these sort of data with doubling survival and we have -- think about cost per quality data, I think this will be relatively favorable.

Now clearly, if the prices are unbelievably high, that's not going to work. But the reality is that because it's transformative and because it's over a clear year of survival, even those organizations had spent a significant amount of money on that.

When you think about sort of second-line approvals with a couple of months here, even EV-301, that overall survival data which was there, a hazard ratio of 0.7, but in the second line set base, that actually number becomes relatively small, whereas here in the frontline space, that data becomes much more powerful because of the huge survival benefit.

Trung Chuong Huynh ***UBS Investment Bank, Research Division - Analyst***

And prostate cancer?

Chris Boshoff ***Pfizer Inc. - Executive VP & Chief Oncology Officer***

A good question. So overall, we're confident we'll get EMA approval for this regimen that's clearly breakthrough regimen for patients with bladder cancer with urothelial cancer.

Thomas Powles ***University of London and Barts Cancer Centre - Professor of Genitourinary Oncology***

Yes, I'd be amazed if that wasn't the case. I'm sure EMA undoubtedly. I mean the question is, as you know, in Germany, it will happen very quickly. It's very likely to happen very quickly in France as well. But I think in the U.K., Spain and Italy, there was a really good chance that this will be approved also because of the transformative nature of the data.

Trung Chuong Huynh ***UBS Investment Bank, Research Division - Analyst***

Excellent. On prostate cancer, TALZENNA is approved in HHR-positive patients in the U.S. In Europe, it's all comers. You mentioned you're going to get the OS data soon. Does that -- and you said with that may come potential additional approvals. Is that you implying that you could potentially get the all-comers label in the U.S.?

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Chris Boshoff ***Pfizer Inc. - Executive VP & Chief Oncology Officer***

Yes, I'll start with that, then I'll ask Roger and also Dana to comment on that. So the approval, you're correct, is in the U.S., but the population in the U.S. is a significant population. It's 30%.

Currently, as Suneet will explain later, we're working on biomarker testing to increase testing for HRR. Others are approved in BRCA only, which is 10% to 11%. We've got approval in 30% of the U.S. population. The overall survival will not just be in the all-comer population, but we'll also get the overall survival data in the HRR population. And that data positive could be used obviously for filings or to enhancement of labels. Roger?

Roger Dansey ***Pfizer Inc. - Chief Development Officer, Pfizer Oncology***

You've said it all, I think. Dana?

Dana Kennedy ***Pfizer Inc. - Therapeutic Area Development Head for Genitourinary Cancer, Pfizer Oncology***

No, nothing to add other than overall survival is a key alpha protected secondary endpoint. It is event-driven, and we're expecting to see results this summer. And if positive, we're hopeful to take those results to negotiate with the health authorities.

Chris Boshoff ***Pfizer Inc. - Executive VP & Chief Oncology Officer***

Go to this side.

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

Chris Schott at JPMorgan. I just had 2 questions on the beta 6 program. Maybe first, can you just elaborate a little bit more on how you see the competitive landscape for ADCs, Trop-2s and how you just kind of see your asset differentiating there?

And then second, as we think about moving into the frontline studies, will you be looking at an all-comer population just PD-L1 highs to try a sense of where you see the most opportunity?

Chris Boshoff ***Pfizer Inc. - Executive VP & Chief Oncology Officer***

Thank you. Good -- I'll start, Megan, if we start and also highlight vedotin again and then Roger to add.

Megan O'Meara ***Pfizer Inc. - Head of Early-Stage Development, Pfizer Oncology***

No, thanks. It's a great question. We're obviously tracking the landscape closely. It's an evolving landscape, and we're confident moving forward into the second to third line space in non-small cell lung cancer in the non-squamous population. We've learned a lot from our Phase 1.

And while there are other ADCs that are working in this space, we see this molecule is quite unique. It's a first-in-class molecule with a target that's highly expressed across a high proportion of non-small cell lung cancer.

And importantly, as we talked about earlier, it has this vedotin payload, which we find to be unique and unique in its combinability in earlier lines of therapy with anti-PD-1. This immunogenic cell death mechanism that we've seen preclinically and now play out in the clinic supports the potential to kind of differentiate in this space potentially compared to the Topo 1 ADCs. Roger, you probably have some more to add?

Roger Dansey ***Pfizer Inc. - Chief Development Officer, Pfizer Oncology***

Yes. And it's -- I obviously agree with everything Megan said. And the promise, I mean, if you look back at obviously single-agent therapy, the landscape has been somewhat mixed. We have a completely different molecule, a completely different target.

We have encouraging initial data. We're running the Phase 3 trial. We'll see how we go. With regard to that frontline opportunity, obviously, for us, if we could repeat the PADCEV experience conceptually because all the science is there, that's what we would love to aim for.

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However, when you get into the details, not even however, like what would a phase -- a frontline trial design be, I think our position right now would be that it would be agnostic to PD-L1 expression number one, driven by the sort of PADCEV, KEYTRUDA experience; and two, driven by our own sort of internal data.

And then the second question is what population because we have to design registration trials that fit into the regulatory landscape. So how do we navigate the regulatory landscape and come forward with a convincing clinical proposition?

So I think speculating on the detail of exactly how we're going to do that is a little premature. But obviously, we have thoughts about it. And we're thinking about what those strategies could be. But clearly, as a sort of bedrock or a foundation to that frontline therapy will be a PD-1 inhibitor together with the ADC.

Chris Boshoff ***Pfizer Inc. - Executive VP & Chief Oncology Officer***

You would have noticed that the second-line trial design was really taken information from Phase 1, focusing on squamous where some of the other competitors have had all comers squamous. And I don't know -- I don't know or non-squamous is not -- or the non-squamous performing bad and the squamous not performing that well. So this is focused on non-squamous.

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

I guess I quick follow-up. Just in terms of a biomarker strategy, is your view of this as kind of broadly enough expressed that's going to be a relevant component to this?

Megan O'Meara ***Pfizer Inc. - Head of Early-Stage Development, Pfizer Oncology***

Yes. I mean we're not prospectively selecting for integrin beta-6 in the Phase 3 study. We have lots of different optionality built in, and we'll be retrospectively looking. We have a comprehensive biomarker plan built into the trial to look retrospectively, and yes. But I think the base case is that we have a large population that we're studying, and we're not perfectively selecting. Roger, do you have anything to add?

Roger Dansey ***Pfizer Inc. - Chief Development Officer, Pfizer Oncology***

Yes. I think on the squamous, non-squamous question, which is an interesting one. Firstly, squamous carcinoma in the lung is an extremely difficult disease to treat. Standard of care isn't very good either.

The data we've generated has pointed us to the non-squamous population, but that doesn't preclude us from still evaluating potentially the squamous population in the frontline. So I would not remove that. It's not off the table.

What's happened in the -- I think, most of the development programs in lung cancer, the delta squamous and non-squamous have created separate trials because the standard of care is different. It gets a bit messy if we're trying to sort of control -- have a nice control arm, but the outcomes are different, and the control arms are different.

So the likelihood, and I'm speculating a little bit here is if we end up entertaining squamous in the frontline, it will probably be its own standalone trial just because of the nature of the disease. And also we'll have to get some conviction about that. So we'll need some data to support that, but I would not say it's off the table.

Akash Tewari ***Jefferies LLC, Research Division - Equity Analyst***

Akash with Jefferies. Can you talk about your subcu PD-1? I feel like there's an obvious incentive to replace KEYTRUDA in all of your bladder cancer regimens with your own internal product. Is there any development strategy that you can talk about bridging studies that we might not be paying attention to right now that could allow that process to get expedited?

And then I guess maybe the pushback on the B6A, I mean, it seems like you're in the same place all the Trop-2 ADCs are, right? Non-squamous in -- you're going against docetaxel. Have you thought about running studies in patients who were previously treated with Topo ADCs? I feel like the issue of cross resistance on ADCs is really not well discussed right now. How are you guys positioning your product with that in mind?

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Chris Boshoff ***Pfizer Inc. - Executive VP & Chief Oncology Officer***

So I'll start with sasanlimab and then ask if anyone wants to add on sasanlimab first. So obviously, first, that is an ongoing Phase 3 trial, as mentioned by Roger. This is a very good PD-1, everything we've seen, subcutaneous designed to subcutaneous is a simple injection once a month.

Initial study that will read out is the Phase 3 non-muscle invasive bladder cancer. The study actually proved very well because the physicians, urologists really liked this simple administration.

It doesn't require like some of the other PD-1s that's now moving to subcutaneous hyaluronidase days, which is a larger injection, more complex. It's very simple. And we use it currently Phase I in various combinations.

And then we'll make a decision if we accelerate any programs into a Phase 3 strategy. Would it remain sasanlimab or should we use for what is a standard of care PD-1 in that specific setting? That is how we're currently thinking of sasanlimab in terms of other tumor types. Roger, anything?

Roger Dansey ***Pfizer Inc. - Chief Development Officer, Pfizer Oncology***

Yes, I think coming from the outside into Pfizer, which I'm excited to do, seeing sasanlimab, sitting there and think, oh, this is a golden egg. I'd like to grab it and use it because it's well configured as well. It's a real PD-1 inhibitor. And it's an obvious partner for the ADCs.

But having said that, it is a complex landscape. And so making choices that we've made so far with sasanlimab focused in bladder cancer is a good place to begin. It fits perfectly with the urology treatment paradigm where they can give subcu.

And so I think the possibility could be that sasanlimab becomes more broadly used certainly in signal seeking. It is much simpler for us to take our own molecules into a signal-seeking trial such as a Phase I on expansion with the combo to understand whether what are PD-1 inhibitors together with another molecule would look like. From a registration perspective, what makes most sense.

I think that's very situational. Like in the moment where we are, what would potentially make the most sense. With regard to how to approach these ADCs with different payloads and different targets, I don't think we're particularly -- the data currently with Trop-2 and the canto payload has not been -- it's not a wow type of outcome.

I think we have an opportunity with our molecule to produce perhaps a stronger profile in that same population. However, if you take something like in HER2, which is obviously an extremely active drug, and it's in a HER2 population, we've got another HER2 ADC with an alternative payload coming behind.

And there, actually, what you're proposing, which is to look at a post one payload and then follow with another payload actually makes a lot of sense. And so we're thinking about that because until people are cured, they will always be cycling into the next therapy.

So I think that's an example where we could possibly. But until something comes along that's really powerful and makes you convinced that your molecule may be better off sort of in a follow situation rather than upfront playing on the same playing field, I think we will continue with the B6A player.

Vamil Kishore Divan ***Guggenheim Securities, LLC, Research Division - Research Analyst***

Vamil Divan from Guggenheim. So maybe a couple on the GU side, first, in prostrate, the member of metastat. You showed the Phase 1 data. I think there might have been a Phase 2 trial either ongoing or you might have some information from. So can you share any of that? Or any plans when do you share that just in terms of the -- that led to the Phase 3 decision.

And then on the bladder side, just HER2 positivity there. We've seen sort of a wide range of numbers. What is your view on sort of the level of HER2 positivity in that cancer type?

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Chris Boshoff ***Pfizer Inc. - Executive VP & Chief Oncology Officer***

Okay. So the first one is actually came in online as well. Online, the questions is the EZH2 Phase 3 trial design based only on the Phase I data or so on Phase 2 data and when we'll see Phase 2 data. Perhaps Dana start with that one.

Dana Kennedy ***Pfizer Inc. - Therapeutic Area Development Head for Genitourinary Cancer, Pfizer Oncology***

Sure. So Roger shared the updated Phase 1 dose escalation data today showing really impressive durability. We're planning to present that at a medical conference later this year in addition to some updated translational data.

We have completed enrollment to a randomized Phase 2 component in the current trial. And we look forward to presenting that data when it's mature. It's really the totality of the data that's driving our conviction to move to Phase 3.

Roger Dansey ***Pfizer Inc. - Chief Development Officer, Pfizer Oncology***

So I mean we are proceeding with Phase 3 trials. Yes, it's important to have all the data available, but we have conviction. We're proceeding.

Chris Boshoff ***Pfizer Inc. - Executive VP & Chief Oncology Officer***

And you also want to answer the second question?

Roger Dansey ***Pfizer Inc. - Chief Development Officer, Pfizer Oncology***

What was the second question?

Vamil Kishore Divan ***Guggenheim Securities, LLC, Research Division - Research Analyst***

HER2 positivity.

Roger Dansey ***Pfizer Inc. - Chief Development Officer, Pfizer Oncology***

HER2. Tom, do you have an opinion?

Thomas Powles ***University of London and Barts Cancer Centre - Professor of Genitourinary Oncology***

Yes. So we ran a big randomized trial in the U.K. with (inaudible) which back in the day, one of the TCRs that didn't work, which 1 of those 23 trials I talked about.

What we were surprised about was how high the HER2 expression was. When you look at (inaudible), then rates are very low. And you look at genetic alterations, the rates are actually low. From an IHC perspective, 1 plus 2 plus 3 plus, we show that over 60% of patients were positive.

And that was -- and I was asked, well, I gave the presentation, it was about 10 years ago. Someone came to the panel like yourself now and said, do you think we should be targeting that? I know patent didn't work, but do you think there'll be other approaches? And of course, being slightly depressed of this big negative trial, I said, no, of course not.

But the answer to the question is yes. And actually, I think it is a good target, and it is widely expressed, surprisingly so.

Chris Boshoff ***Pfizer Inc. - Executive VP & Chief Oncology Officer***

Do you want to add to that?

Roger Dansey ***Pfizer Inc. - Chief Development Officer, Pfizer Oncology***

I think our epi data -- we agree with Tom. I think our epi fdata would put it in that sort of 50% range, something like that.

Chris Boshoff ***Pfizer Inc. - Executive VP & Chief Oncology Officer***

That include HER2 low.

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Roger Dansey ***Pfizer Inc. - Chief Development Officer, Pfizer Oncology***

Yes, that's with HER2 low. So just then the nomenclature, the traditional HER2, which would be overexpressed or amplified. It's probably around about 15%, something like that. And then the rest going up to around 50% would be in that IHC 2 and not-ish IHC 1, something like that. But it is a pretty prevalent biomarker in bladder cancer.

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

Steve Scala, TD Cowen. Two questions. First one is a little bigger picture. You started the presentation this morning by noting that your Oncology business grew 19% in the last decade, and that was about twice the industry average. But that was a period when Pfizer had a lot of growth in oncology products, and your competitors had quite a few LOEs. The reverse is true in the next decade.

So what do you think your Oncology business can grow in the next 10 years? And how does that compare to the industry average? So that's the first question.

Second question is in the EV-302 trial, Pfizer mentioned, I think, that a significant portion of the controlled patients were on the avelumab. Can you clarify how the PADCEV plus KEYTRUDA patients compared to the alvalumab plus chemo patients?

Chris Boshoff ***Pfizer Inc. - Executive VP & Chief Oncology Officer***

Okay. Two very good questions. We'll start actually with the second one with avelumab and the number of patients, which in the study looked like the real-world data, what we saw the number of patients on avelumab. Tom?

Thomas Powles ***University of London and Barts Cancer Centre - Professor of Genitourinary Oncology***

So it is a good question, and it's one which we've been discussed in many forms. The trial always allowed avelumab patients to take part. The amendment that took place during the trial was just that we didn't count -- if they started avelumab, historically, we would count that as a new therapy and that we call sensoring and sensoring is bad for PFS. So we changed so that avelumab will be considered as first-line therapy.

When we looked at avelumab uptake in the study, 31% of patients got maintenance therapy. When you look at real-world data for avelumab, the number is somewhere between 20% and 30%. That's probably a bit on the low side, and that might be representative of people not being super keen to use it for whatever reason. I don't want to discuss the detail of that too much today.

In the context of a clinical trial, I would expect that probably to go up to more like 40% or 50%. One -- on the Twitter poll on that, I ask my colleagues, and it came out between 45% and 50%.

The 31% is much higher than, for example, the 901 trial. It was down at 15%. When you look at the performance, the control arm, it's about 16 months median survival, historical 12 to 13 months for all comers, including cisplatin eligible and ineligible. And so therefore, it is performing a bit better than you'd expect, and that's probably represented a little bit of that.

Even the best-case scenario, if everyone of 50% of patients have got avelumab, the median survival advantage is 25%. So you divide that by 2 to about 12%. And then you think, well, actually you don't start at the beginning. They start halfway through, so that 12% goes down to about 8%.

So you could say, okay, and half of our patients got avelumab. So that comes about 4% or 5%. So maybe you'd take 5 points off that hazard ratio, so instead of 0.45, it's 0.5. So I don't think it's a massive impact. And I think all my colleagues agree with that.

Chris Boshoff ***Pfizer Inc. - Executive VP & Chief Oncology Officer***

And then for the first part of your question, in the commercial session this afternoon, we'll expand on some of the commercial opportunities. You've heard already about 3 or 4 of our medicines, which we believe could be significant growth in the next up to 2030 and beyond. And this afternoon, after the break, you'll hear of another 4 or 5 of these, and then we'll expand on your question. But we believe it's more than enough to make up for the LOEs that's coming from oncology.

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

Louise Chen from Cantor. So first question I had for you is given that the EV-302 data came up better than anticipated, how do you think it would add to the sales aspirations you have given for Seagen?

And second question is on EZH2. Just curious, ultimately, where would you like to fit into the treatment paradigm as you advance your program here?

Chris Boshoff ***Pfizer Inc. - Executive VP & Chief Oncology Officer***

So on the first -- I'll start with the first one on 302. Again, we'll provide additional color, Suneet in his presentation this afternoon. We're obviously very excited by the data. The early data we've now seen, we see the growth as expected from the transformative data, both in the community setting as well as in academic setting.

And actually, what Suneet will show later is after the 70% account that they used was PADCEV. PADCEV is in the community setting. We have not changed guidance for Seagen. And currently, it is what we said it before, approximately 10 billion additional by 2030. But we haven't changed it in view of the PADCEV data. Roger, do you want to add?

Roger Dansey ***Pfizer Inc. - Chief Development Officer, Pfizer Oncology***

Yes. And I think Dana may chime in as well. So for me, again, relatively new to the program, I would see the EZH2 inhibitor churn is just the beginning. If you look back, and it's really hats off to Pfizer for developing XTANDI the way it was, taking on early populations, long trials, but really making a difference.

And I think you can extrapolate. You could say, okay, if we can get the EZH2 inhibitor with a good profile, both efficacy and safety and tolerability, there's nothing stopping us from building another wall of data now with an EZH2 inhibitor on top as appropriate.

So that would be my -- but of course, we're beginning life with these 2 trials. And when they read out, I think we'll have a good idea of, yes, this is something we should jump on and expand further. Do you...

Dana Kennedy ***Pfizer Inc. - Therapeutic Area Development Head for Genitourinary Cancer, Pfizer Oncology***

I completely agree. We're building on the backbone of XTANDI as we think about the development of EZH2 in prostate cancer. And there's a lot of biologic rationale for why an EZH2 inhibitor would combine well with an antigen receptor inhibitor like XTANDI.

Simply put, combining our EZH2 inhibitor with XTANDI helps XTANDI work again and work better. And we want to continue to build in prostate cancer to improve outcomes for our patients.

Chris Boshoff ***Pfizer Inc. - Executive VP & Chief Oncology Officer***

Thank you. Andrew?

Andrew Simon Baum ***Citigroup Inc., Research Division - Global Head of Healthcare Research and MD***

Andrew Baum, Citi. Apologies for the voice. So 3 quick questions. First one for Roger. When you were at Merck, you carpet bombed every indication with KEYTRUDA. It looks like AstraZeneca hasn't successfully done that within HER2, at least in HER2 low non-breast. So given and assuming you have activity in HER2 low, why not actually pursuing other indications outside breast for that patient population? Is that the intent? That's one.

Second question for Megan. You described it as synergy. I would argue on response rates, I could use the word additive instead of synergy.

And the final question to Chris. On your SHP2 inhibitor to address TKI resistance, could you talk to your level of excitement about that, given some of the early data that was published?

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Chris Boshoff ***Pfizer Inc. - Executive VP & Chief Oncology Officer***

Thank you. So we'll start with Roger, carpet bombing and then...

Roger Dansey ***Pfizer Inc. - Chief Development Officer, Pfizer Oncology***

Yes, I think I completely agree with you. I mean the DV story is also just beginning. I think we've -- we took the data from China, and that was where the Chinese program had begun as breakthrough therapy designation with the FDA. So it was very easy for us to just say, yes, that's where we'll go, high expression.

PADCEV led the way in terms of like understanding will an ADC work, they had data. So the urothelial story is easy to tell. But as Chris told you, it's approved in China for gastric cancer. I think when we get our arms more around DV and the opportunity, there are multiple other places that we can go. So I don't think that story is completely told.

In terms of what drives an ADC outcome that is good in one tumor and bad in another, it would be nice to have researchers comment on this, but from a simple perspective, if the target isn't changed, and you change the payload, then the outcome is driven by payload sensitivity. And so different tumors differently -- are differentially sensitive to things like Topo 1s and tubulin disruptors. So I think the tubulin disruptor will find its home where the tumor is sensitive and the target works.

In other words, it internalizes correctly and delivers the payload into the cell where it needs to be. But it's a long answer for a relatively straight thing, which is the DV plans are not completely fleshed out, and we need to understand where else we can take it.

Chris Boshoff ***Pfizer Inc. - Executive VP & Chief Oncology Officer***

Then Megan?

Megan O'Meara ***Pfizer Inc. - Head of Early-Stage Development, Pfizer Oncology***

Sure. So fair point, I think there is a preclinical definition of synergy that's different than what we were talking about here, which we said potential clinical synergy, and it's really looking at the totality of the data. If you look across our vedotin experience combining with PD-1, you look at the response rates, if you look at the durability and you look at the long-term time to event endpoints like survival like we saw with PADCEV, we believe there's something unique about this -- the immunogenic cell death mechanism and PD-1. And it's played out both in the labs preclinically and then in the clinic.

Chris Boshoff ***Pfizer Inc. - Executive VP & Chief Oncology Officer***

Yes. And I think just a point about that is not just its durability.

Megan O'Meara ***Pfizer Inc. - Head of Early-Stage Development, Pfizer Oncology***

Durability.

Chris Boshoff ***Pfizer Inc. - Executive VP & Chief Oncology Officer***

It's really...

Andrew Simon Baum ***Citigroup Inc., Research Division - Global Head of Healthcare Research and MD***

I was just -- because you showed the response rate.

Megan O'Meara ***Pfizer Inc. - Head of Early-Stage Development, Pfizer Oncology***

It's a fair point.

Chris Boshoff ***Pfizer Inc. - Executive VP & Chief Oncology Officer***

That's a fair point.

Roger Dansey ***Pfizer Inc. - Chief Development Officer, Pfizer Oncology***

Lot of elements.

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Chris Boshoff ***Pfizer Inc. - Executive VP & Chief Oncology Officer***

Yes. It's just looking at responses you can argue is additive or adding to it, but I think its durability, depth of responses as well, durability and then the overall survival data. But it's fair enough point.

I think the main thing is that, that payload elicits something we haven't really seen yet, although we'll present this opportunity some of the Topo 1 going in the clinic as well and what's not in the clinic with us. We haven't seen that immunogenic cell death to that extent yet with outside of MMAE. Your last question was regarding...

Andrew Simon Baum ***Citigroup Inc., Research Division - Global Head of Healthcare Research and MD***

SHP2.

Chris Boshoff ***Pfizer Inc. - Executive VP & Chief Oncology Officer***

SHP2, yes. So Jeff will briefly mention SHP2 this afternoon. Our SHP2 looks differentiated at the moment. We know the SHP2, as you know, the 2 or 3 that's in the clinic has been challenging in terms of side effects, and we don't see that. So we do believe we potentially have a best-in-class SHP2.

You're absolutely correct. Preventing resistance to TKI could be one way forward with the SHP2. We actually have an ongoing study with lorlatinib, but now starting to look at the data, the long-term follow-up with lorlatinib, which appears unprecedented. You may not need a SHP2 for lorlatinib. It's doing something very different than what we've ever seen before with the TKI. But fair point on the SHP2.

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

Evan Seigerman from BMO. So a follow-up to the earlier question on chemotherapy in the second line in lung. What have you done in your trial with -- I'm going to call it, SV to ensure that you're going to get the maximum benefit of the drug versus standard-of-care chemo, which we've seen surprise over and over.

Last month, we had a surprise trial with another ADC where the trial didn't work. And then a follow-up to that. In the front line, pembro, chemo works really well. What are you doing again to design that trial to show benefit in this -- in that setting?

Chris Boshoff ***Pfizer Inc. - Executive VP & Chief Oncology Officer***

So we'll start with Megan and then -- and Roger. I also mentioned the endpoints of the trial, which I think is very well designed.

Megan O'Meara ***Pfizer Inc. - Head of Early-Stage Development, Pfizer Oncology***

Yes, yes. Thanks. I mean -- so sorry, no, I'm like, what was the first part of the question. Remind me.

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

Second line, really -- actually derailed some trials that we thought would have been successful.

Megan O'Meara ***Pfizer Inc. - Head of Early-Stage Development, Pfizer Oncology***

So we've really tried to be data-driven with our design. We -- in a Phase 1 study, we enrolled a very heavily pretreated lung cancer population. And so we looked at a number of prior lines of therapy. We looked at taxane exposure. We looked at non-squamous versus squamous. And we've enrolled quite a few patients in the Phase I.

You'll see later this year when we present more of the data. And we feel confident based on our review of the Phase 1 data that this Phase 3 is a very data-driven design based on what we've seen for the best chance of providing the best clinical benefit for patients in the second to third line setting versus tosetaxel.

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

Okay. And I guess along those lines, where are you getting all of this data? I know you look at your competitors in New Jersey. They've been generating data for a decade when it comes to making the standard of care. And I want to ensure that you have the most accurate, kind of most comprehensive data set.

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Megan O'Meara ***Pfizer Inc. - Head of Early-Stage Development, Pfizer Oncology***

Are you talking about for the control arm?

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

Just the control arm, right? They know how pembro works. They know how chemo works in all these lines. And I think that's kind of one of their bits of secret sauce.

Megan O'Meara ***Pfizer Inc. - Head of Early-Stage Development, Pfizer Oncology***

Well, luckily, from the second to third line setting, we have several very recent trials that have read out in the docetaxel space, including the patients that have been exposed to prior PD-1s. And we've done our homework at looking at meta-analyses when we've done -- kind of worked up the biostatistical design of the Phase 3. So I think we're confident based on that, that we feel like our estimates are accurate from a very recent historical control perspective. Roger?

Roger Dansey ***Pfizer Inc. - Chief Development Officer, Pfizer Oncology***

Yes. No, I think we're accounting. If you're saying the control arm keeps getting better, we're accounting for that apparent improvement in the control arm.

With regard to the first-line design, I try to allude to some of the sort of design principles and concepts and strategies around how to get there. And for sure, in lung cancer, combining a PD-1 inhibitor with chemotherapy does have some amazing outcomes. I've lived that personally.

Not true for all cancers. I mean clearly, in urothelial cancer, that same plan did not work. So there's something not surprising. We don't know everything about what we do. There's something about lung cancer that sets up a good interaction between the chemotherapy treatment and the PD-1 inhibitor.

But I would say, again, I think for us, the Holy Grail is to try and repeat the PADCEV, KEYTRUDA experience with another molecule in another disease. And the simplest proposition for treaters and for patients would be to have a doublet to basically take an ADC, put it together with a PD-1 inhibitor and get an outstanding result. And that would be probably the best outcome we could expect.

And that would be against, obviously, the trials that have to run against the current standard of care. So the bar would be very high. That's why in order for us to undertake that, we need to get to a place where our data supports that type of approach.

Beyond that, beyond the simple doublet approach, it would then be adding in another chemo. It will become like a replacement strategy, pull out a chemotherapy agent, replace with an ADC and then do sort of a HER2 comparison with a replacement plan. And those are the 2 basic options that's sort of in front us in the frontline setting. And I think when we're ready to share, when we've got the information we need and we've come up with a design, we'll obviously bring it forward.

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

Terence Flynn, Morgan Stanley. A question for Dr. Powles, a crystal ball question. There's a lot going on in earlier line bladder when you think about what J&J is doing with their Taris device. You mentioned moving PADCEV to earlier lines. You have a CG oncology product, a gene therapy product. So as you look across these different platforms and opportunities, how are you thinking about putting those to use in your practice if they all become available? Because it seems like it is getting increasingly more crowded there.

Thomas Powles ***University of London and Barts Cancer Centre - Professor of Genitourinary Oncology***

It's a good question. And I don't know the answers. Obviously, I'm going to do a little bit of guessing if I may, but I wouldn't hold me to it.

Having said that, I think EV pembro is likely to make a big difference in the preemptive space. If we get anywhere near what we did with gem/cis beating that in metastatic disease, we put that into muscle-invasive space.

I think that's going to make a big difference in the short term. In the muscle-invasive space, there's a study called (inaudible), there is a

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study called (inaudible). They're both looking in that first-line non-muscle-invasive setting. I think they're both important studies.

I think the subcut approach does appear attractive to me for what it's worth. I think urologists are going to be very reluctant to give IV therapy. They just haven't got a track record of doing that, don't think they will do it actually.

And so there's an opportunity there. I agree completely. I think you look at TAR200, TAR210, the J&J program and muscle -- in the non-muscle-invasive space. I see that being competitive as well. I see the whole field moving very quickly.

And what I think is really exciting about it, I think there's really 0.5 million deaths in bladder cancer globally every year. I think we can reduce that by half over the next 5 or 10 years by some of the programs that have been talked about today and some of the other programs that you've highlighted. But that J&J thing, I agree with you.

Chris Boshoff ***Pfizer Inc. - Executive VP & Chief Oncology Officer***

That's a good question. Urologists still like to use BCG, very important for urology practices in the U.S. So adding something simple like a subcutaneous once-a-month injection, if that study is positive, we believe it's going to be significant uptake for non-muscle-invasive.

Courtney Breen ***Sanford C. Bernstein & Co., L.L.C. - Senior Research Analyst, US Biopharma***

Courtney Breen from Bernstein. Just 2 questions. One for Thomas over there. As you think about EV, you mentioned that in some cases, you're using only 4 or 5 doses and getting a durable response. So as you think about kind of the real-world use of this product, can you give us a bit of a signal as you think about what types of patients may end up with perhaps shorter utilization of the product and what perhaps an average in the clinic might look like?

Thomas Powles ***University of London and Barts Cancer Centre - Professor of Genitourinary Oncology***

So I think that's a really good question. And I've got quite a lot of personal experience of EV, and I speak about it to friends and around the world and colleagues. And so I think the feeling at the moment is that the majority of patients can get 10 cycles. There is a real skill to giving these chemotherapy type drugs. We've learned that skill. 6 cycles of -- no one gets 6 cycles of gen/cis. There's a delay, there's a reduction.

So we're very skilled at that in the bladder cancer community. And that's exactly what we're doing with EV at the moment. And we've recently audited our cohort of patients, and everyone is a bit different. And what happens is some patients start, they get 10 cycles, they go through without any problems. They come in and say, listen, I really want to have a break, want some time off.

And they're having deep durable responses. And I think what's really exciting is some of those patients and we stop, the cancer doesn't come back. I don't think it is the EV pembro, you have to have it. And if you stop it, everything bounces back because we're causing these deep responses, the pattern is very different from what we've seen before. That's number one.

And then the second important piece is that people talk about the skin toxicity and the peripheral neuropathy. But when you have -- if you get early skin toxicity and you delay and you dose reduce and you come back in 2 or 3 weeks later, you can rechallenge at one dose down.

And what we found is you can keep going for a long period of time on that, and it doesn't reintroduce that skin toxicity. That's really important. And the last issue I'd like to talk about the peripheral neuropathy. People talk about that. They say you can't get beyond 10 cycles. That's not our experience at the moment either.

Our experience again is as soon as -- grade 2 peripheral neuropathy is really quite significant. And what we found is if you intervene a grade 1, you bring the dose down, you lay by 2 or 3 weeks and you've got that lower dose, you can keep giving the drug.

So there's a lot of education and training that we need to do in this. But I don't think that the simple principle, you give the drug and then you have to stop then you run into problems, that's not the experience that we are seeing at the moment.

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Courtney Breen ***Sanford C. Bernstein & Co., L.L.C. - Senior Research Analyst, US Biopharma***

And the follow-up was just on the PD-L1 ADC. Just a couple of questions there. We've seen with PD-1s versus PD-L1s when it comes to the mabs. I'd love to understand why you're going after the ligand.

And then secondarily, kind of as you think about the tumor types to begin kind of expanding this and why not something more immune-sensitive like lung or melanoma? Why go for head and neck?

Chris Boshoff ***Pfizer Inc. - Executive VP & Chief Oncology Officer***

Good question on PD-L1 ADC.

Megan O'Meara ***Pfizer Inc. - Head of Early-Stage Development, Pfizer Oncology***

Sure. So to answer your first part of your question, we're going after the PD-L1 target because that's the part of the interaction that's expressed on the tumor cells. And we see this really straight up mostly as an ADC that's delivering a potent or a stent payload into the tumor cell, leading to direct cytotoxicity by standard effect and immunogenic cell death.

So it's not necessarily the main -- we don't believe that the main mechanism of action here is checkpoint blockade but rather delivery of a cytotoxic payload. And as you know, there's a broad range of tumor types that express PD-L1.

We designed the trial not just to look at head and neck cancer. We're also looking at many other PD-L1 expressing tumors that we know to be sensitive to a microtubular-disrupting agent and are more likely to express PD-L1. And so we're enrolling other tumors, non-small cell lung cancer, esophageal cancer, triple negative breast cancer as well.

And so it's not just head and neck. It turns out that we -- there's a very high medical need in head and neck cancer. And so a lot of the patients that came on the study early had head and neck. Yes.

Chris Boshoff ***Pfizer Inc. - Executive VP & Chief Oncology Officer***

And just to add to that, and Scott Peterson will discuss this afternoon as well. This dose that's given is too small to block the PD-1 access. So you still need an immune checkpoint if you want to use it as an immune medicine. This is just the target because PD-L1 being expressed highly on tumor cells.

Good question. We've got online -- we'll just go online. There are large unmet need in RAS-mutated colorectal cancer and also in platinum-resistant ovarian cancer. Are you looking at solutions for these large patient populations?

We mentioned in RAS, we want to continue to stay focused on our tumor areas. But in colorectal cancer, we mentioned that we do have 2 ongoing Phase 3 studies that should both read out in the next 12 months. One is in the BRAF first-line colorectal cancer in combination with Cetuximab and doublet chemotherapy. And the other is in first-line HER2-positive colorectal cancer where tucatinib is combined with trastuzumab and doublet chemotherapy.

Combined if those studies are positive, and we actually have great confidence in those studies, so the data that was generated in Phase 1/2, that will cover up to 15% of colorectal cancer. So that's our focus at the moment for colorectal as a targeted approach with tucatinib and with Braftovi.

Roger Dansey ***Pfizer Inc. - Chief Development Officer, Pfizer Oncology***

Have CCAM5.

Chris Boshoff ***Pfizer Inc. - Executive VP & Chief Oncology Officer***

Perhaps add something on CCAM5, although we'll discuss this afternoon again, but if you want to mention...

Roger Dansey ***Pfizer Inc. - Chief Development Officer, Pfizer Oncology***

So we have other possible players as well. But this presentation is focused on the big fish for the moment is we...

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Megan O'Meara ***Pfizer Inc. - Head of Early-Stage Development, Pfizer Oncology***

The early pipeline you'll see in a bit, we've got broad opportunities across large patient populations beyond what you've seen so far.

Roger Dansey ***Pfizer Inc. - Chief Development Officer, Pfizer Oncology***

If you got another 2 days, we could keep talking.

Chris Boshoff ***Pfizer Inc. - Executive VP & Chief Oncology Officer***

We'll now take a break for approximately 30 minutes and then start again with our session on breast cancer, hemato-oncology and our next-generation opportunities as well as our commercial perspectives. Thank you. Just on the right, if you go out, it's on the right side is coffee and drinks. Thank you very much. See you in 30 minutes.

(Break)

PRESENTATION

Chris Boshoff ***Pfizer Inc. - Executive VP & Chief Oncology Officer***

Welcome back, everyone. I hope you enjoyed the break. We'll now turn our attention to breast cancer. Pfizer has a legacy, as you all know, in breast cancer, spanning more than 2 decades with strong foundation in research and development of 2 key approved medicines. In a few moments, I'll ask Roger Dansey to share our development plans which have the potential to expand significantly our portfolio in breast cancer and bring forward potential new breakthrough treatments for breast cancer.

Breast cancer is the most common tumor type among women in the United States with 1 in 8 women receiving a diagnosis during their lifetime. It caused an estimated 44,000 deaths in 2023 alone. While early breast cancer can often be cured, many patients progress to advanced metastatic disease, which remains incurable. We're very proud of having introduced to the world the first CDK4/6 inhibitor, IBRANCE, which has been a transformative therapy for hormone receptor-positive human epidermal growth factor negative metastatic breast cancer.

Since its approval in 2015, IBRANCE had been a market-leading CDK4/6 inhibitor and has treated over 665,000 patients globally. We see significant opportunity in breast cancer, which currently is a $30 billion global market that is expected to reach $60 billion in 2030. We are confident that with our differentiated pipeline, deep expertise and strong relationships with the global breast cancer community, we are poised to not only continue but strengthen our leadership in this space.

I'll now invite Roger back to speak more about our development plans in breast cancer, including 7 -- several potential near-term catalysts. Thank you.

Roger Dansey ***Pfizer Inc. - Chief Development Officer, Pfizer Oncology***

Yes. Thanks very much, Chris. Again, I mean, this is an exciting opportunity for us. I mean breast cancer, it has a huge impact in the world, and it's a key focus for us. So we're committed to improving breast cancer outcomes wherever and whenever we can. So it is a collection of multiple diseases.

So if you look at the pie chart on the left of the slide, you can appreciate that the hormone receptor-positive, HER2-negative subtype comprises around 70% of all breast cancer cases, so a very large fraction. And then HER2-positive, the sort of traditional version of HER2-positive anyway, and triple negative breast cancer comprise the remainder. So in hormone receptor-positive, HER2-negative breast cancer, beyond the approved product, IBRANCE, our pipeline actually includes 4 promising candidates, 4 promising molecules, including 2 that are already in Phase 3 development.

And now with the addition of TUKYSA and several early-stage ADCs, as you can see on the slide, we now have the opportunity potentially to address the other subtypes, not just limited to the hormone receptor-positive group. So in this presentation, I'm going to focus the 2 late-stage molecules, hormone receptor-positive breast cancer, that's atirmociclib, our highly selective CDK4 inhibitor; and vepdegestrant, the only PROTAC estrogen receptor degrader that's currently in clinical development.

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I'll also be discussing TUKYSA, this remarkable CNS penetrant, HER2 TKI, where we actually have active trials in earlier lines of breast cancer beyond where TUKYSA has already been studied. And the clinical-stage ADC, I think you heard earlier from Tom around disitamab vedotin, and we had some discussion in the Q&A. The full DB plan is not necessarily being presented here.

But clearly, we are interested in HER2-positive tumors, whether it's breast cancer, gastric cancer or other cancers beyond urothelial cancer. And Jeff Settleman in discovery research will talk about felmetatug vedotin, otherwise known as B7H4, along with our potential first-in-class KAT6 inhibitor, a novel CDK inhibitor. I hope you can appreciate on this slide, we bring lots of potential to the breast cancer space.

So turning to our efforts for next-gen therapies for hormone receptor-positive breast cancer. While the combination of CDK4/6 inhibitors with hormone therapy is the gold standard of treatment for hormone receptor metastatic breast cancer, not all patients respond adequately and most ultimately progress and receive systemic chemotherapy. So there is a need to improve upon the existing therapies.

And with atirmociclib, we believe we have the potential to continue our leadership that we've established with IBRANCE, now introducing a new cell cycle inhibitor backbone that we think offers more complete and continuous CDK target coverage, CDK4 target coverage with improved tolerability. And with vepdegestrant, which we are co-developing with Arvinas, our aim is establish in the same conceptual way a new standard of care, endocrine therapy backbone. And that's based on data which I'll share, impressive activity for vepdegestrant regardless of ESR mutation status. And that ESR-mutant status actually is a common driver for resistance to current endocrine therapy.

So it is important to note that we have comprehensive development plans and programs for both of these molecules, and we plan to study the entire treatment continuum. So let me walk you through some of the data that underpins our confidence in these molecules. So I'll begin with atirmociclib and the prospect of creating a molecule that specifically target CDK4 while sparing CDK6 has been a challenge that our medicinal chemists have been working towards for a number of years. And we now have it in atirmociclib. This is a molecule that can potentially maximize the efficacy through selective CDK4 targeting while minimizing toxicity by sparing CDK6 and other kinases.

There are some important biochemical attributes of atirmociclib which potentially differentiates it from CDK4/6 inhibitors. In the upper half of this slide, you can see kinome screens, which show the results from over 270 activity assays for the current CDK4/6 inhibitors and atirmociclib. Just to orient you, if you're not familiar with these, the red dots depict regions where the molecules are most active, and the boxes focus on where the CDK4/6 -- CDK4 and CDK6 domains reside. In the atirmociclib tree, all the way on the right of the slide, you can see almost exclusive activity in the CDK4/6 region with no meaningful off-target activity elsewhere.

And with regard to selectivity for CDK4, if you look in the box below the kinome trees, atirmociclib has the highest selectivity amongst these molecules with a 33-fold ratio of favoring CDK4 over CDK6. So essentially, this is a CDK4 inhibitor. So there's lots of preclinical evidence to suggest that the clinical data could point in the direction of better efficacy and potentially better tolerability. And I'd like to walk you through this data, which is updated from a Phase 1 study evaluating atirmociclib in combination with endocrine therapy.

And it's important to note, as is often these initial studies, this -- patients in this study had received a median of 4 prior lines of therapy. 100% had received a prior CDK4/6 inhibitor, and most having received prior chemotherapy and prior fulvestrant. The overall response rate was an impressive 32%, and this is in a population where the benchmark would be less than 10% with available endocrine-based therapies.

And if you look at the Kaplan-Meier curve on the right of the slide and out of this data set, the median progression-free survival observed at the time of data cutoff was 8.1 months. Again, in an indirect way but it's the only way we can with single-arm data, the benchmark would generally be under 4 months. So this is impressive initial data. So not just the efficacy but safety and tolerability, atirmociclib has the potential to differentiate. There have been no head-to-head studies between atirmociclib and CDK4/6 inhibitors. But the available safety and tolerability data points to where atirmociclib may offer advantages.

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Starting with neutropenia. As you can see on the slide, consistent with its selectivity for CDK4 and not hitting CDK6, atirmociclib plus fulvestrant appears to cause a lower incidence of neutropenia, including the higher grades, where things potentially can go wrong for patients. So that's an important potential differential. And the numbers are quite different. With regard to GI side effects, atirmociclib also appears to have a low instance of severe diarrhea. And that's basically because it's not a multikinase. It hits a very restricted kinase panel.

And so probably most importantly, most notably as a measure of tolerability, we see very few dose reductions due to adverse events and with a low single-digit rate of discontinuation. I can tell you just as I've been developing drugs for a long time, getting low single-digits discon means a highly tolerable drug that can be used potentially for prolonged periods of time. And while these numbers are limited in terms of how many patients have we studied, the data does support the potential for atirmociclib to be dosed in that more complete and continuous fashion, which is critical in a disease state where prolonged therapy actually is required because fortunately, the time lines for patients with breast cancer are long before something potentially goes wrong.

So based on these data, we are working to develop this molecule across both early and late hormone receptor treatment settings. So starting from the left, we are currently enrolling a Phase 3 registrational study, which is evaluating atirmociclib plus fulvestrant compared to physician's choice of fulvestrant or everolimus plus exemestane in the metastatic post-CDK4/6 setting. This trial is anticipated to read out in late '25 or early '26. So we've begun this journey in that post-CDK4/6 setting.

In parallel, we are planning to execute a frontline Phase 3 registrational trial which will evaluate atirmociclib plus an aromatase inhibitor versus physician's choice, our CDK4/6 plus an aromatase inhibitor as well. And obviously, this is at a very high level what we are thinking of doing, and more details to come as we get closer to that. But we look forward to initiating the study in the second half of this year.

And in parallel, we are also advancing atirmociclib for potential use in early breast cancer, and we plan to initiate a signal-seeking trial in that -- in the second half of 2024. We will combine atirmociclib with an aromatase inhibitor, essentially a window of opportunity type of study. We believe that the development program that I presented to you has the potential to position atirmociclib as that replacement for CDK4/6 inhibitors across all lines of hormone receptor breast cancer settings and -- breast cancer settings and lines of therapy.

So let's turn now to vepdegestrant, which is the first PROTAC ER degrader in clinical development. PROTAC, by the way, stands for PROteolysis Targeting Chimera and is a unique mechanism of action compared to other ER-targeted therapies. Vepdegestrant degrades and removes both the wild-type and mutant estrogen receptors to effectively interrupt signaling. And as mentioned earlier, ER mutations are actually a common cause of acquired resistance to endocrine therapy.

While not sharing this with you today, we've been very pleased with the clinical data generated for vepdegestrant as monotherapy in heavily pretreated patients. But I will share with you some of the investigational combination data where we've combined vepdegestrant plus IBRANCE, and we have demonstrated compelling antitumor activity in heavily pretreated patients with locally advanced or metastatic ER-positive, HER2-negative breast cancer.

Shown here on the next slide are the interim data presented at the San Antonio Breast Cancer Symposium just a couple of months ago. And the population study is heavily pretreated, median of 4 lines of prior therapy, 87% receiving prior CDK4/6 inhibitors. And if you look at the waterfall plot on the left, you can see most patients in the circumstance combining vepdeg with IBRANCE experienced tumor shrinkage. So in this initial evaluation, the overall objective response rate was 42% in a population, again, where response rates will generally be considered to be less than 10% with the standard endocrine-based therapies.

And then looking at the outcome by the ESR1 mutation status, we basically see comparable response rates in both the ESR1 mutant and wild-type tumors, which is also very encouraging as a potential added attribute of this molecule. And then looking at the Kaplan-Meier curve, we are equally encouraged by the median PFS of 11 months. But again, the benchmark is generally less than a 4-month period with existing therapies. So vepdegestrant and IBRANCE also demonstrated initial manageable safety and tolerability, but we are continuing to optimize the IBRANCE dose for use in this combination.

And if you look at the chart on the left, the treatment-related adverse events observed were consistent with the known safety profile of

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IBRANCE in combination with endocrine therapy and the safety profile observed in studies to date with vepdeg monotherapy. Neutropenia was observed frequently in this combination study, likely related to higher-than-expected exposure to IBRANCE but was nevertheless still effectively managed through standard IBRANCE dose reductions. And importantly, the dose-reduced IBRANCE population in this combination was associated with durable responses with a median time on treatment of 36 weeks once the dose was reduced.

So I think overall, these combination results as well as the previously disclosed vepdegestrant monotherapy data have given us confidence to move forward with this molecule with multiple development strategies. Our intention, again, is to develop vepdegestrant as the backbone ER-targeting therapy, including in frontline and early breast cancer settings, and we have a number of ongoing and planned trials to support this approach.

Let me begin on the left with registration-intense studies in the second-line metastatic setting. First, we have the ongoing Phase 3 VERITAC-2 study, which is evaluating vepdegestrant as a monotherapy, sufficient activity to evaluate as a monotherapy versus fulvestrant with an anticipated readout in the second half of 2024, so pretty proximal to today. And subject, obviously, to clinical trial and regulatory success, we could anticipate that monotherapy would be the market entrant indication and potentially establishing vepdegestrant as their best-in-class novel endocrine therapy in late-line disease.

And given the importance of combination therapy in more advanced aggressive disease, we are also planning a registrational study with vepdegestrant plus a CDK4/6 inhibitor versus standard of care in the second-line post-CDK4/6 setting. And we anticipate starting this study in 2025. In frontline metastatic breast cancer, we aim to establish this new backbone endocrine therapy concept. And as mentioned earlier, we are optimizing the dose of IBRANCE in combination with vepdegestrant to manage things like the neutropenia. And that's in a study lead-in for the VERITAC-3 trial, which is also currently enrolling.

And in parallel, we are evaluating the safety and tolerability of a combination of vepdegestrant and atirmociclib, the 2 novel agents, in a Phase 1b study that is also enrolling. So data from this VERITAC-3 trial, the safety lead-in, in combination with IBRANCE, data from the Phase 1b/2 study of vepdegestrant in combination with atirmociclib will continue to inform the precise registrational path for vepdegestrant in the first-line metastatic setting. And we anticipate making a data-driven decision this year and initiating a Phase 3 trial in 2025. Finally, we have an ongoing Phase 2 signal-seeking trial of vepdegestrant versus AI in the neoadjuvant setting. And that, too, has an anticipated readout in 2024.

So moving now on to TUKYSA, our best-in-class tyrosine TKI for HER2-positive breast cancer. As we know, HER2-positive tumors are biologically more aggressive and are associated with poor survival compared with HER2-negative cancers. And one of the hallmarks of HER2-positive breast cancer is the development of brain metastases in upwards of 50% of patients with the condition over the course of their disease. And owing to its high selectivity for HER2 and remarkable brain penetrants, TUKYSA has demonstrated an overall survival benefit and strong CNS activity in HER2-positive breast cancer.

Shown here are the efficacy results from the pivotal HER2CLIMB trial, which was unique in that nearly half the patients enrolled had brain mets, including those with active disease. HER2CLIMB evaluated TUKYSA in combination with trastuzumab and capecitabine in patients who received prior treatment with trastuzumab, pertuzumab and T-DM1. Focusing first on the chart on the left, you can appreciate the statistically significant and meaningful survival benefit with TUKYSA with the risk of death reduced by 34%.

Looking at the Kaplan-Meier curve on the right, there was a clear benefit for patients with brain metastases with a 52% reduction in the risk of progression or death. HER2CLIMB also demonstrated favorable safety, low discon rates and no requirement for prophylactic anti-diarrheal medication, which is commonly used with less selective HER2 TKIs. So based on these results, we believe TUKYSA is a best-in-class TKI therapy for patients with HER2-positive breast cancer, and we aim to extend its benefits to earlier lines of treatment.

We're continuing to develop TUKYSA as a backbone TKI in HER2-positive breast cancer and are particularly excited by the potential opportunity to delay or even prevent the development of brain metastases in earlier lines of therapy. HER2CLIMB supported the initial approval in 2020 in that second-line-plus metastatic setting. And more recently, HER2CLIMB-02, which was also presented at San Antonio, demonstrated that you could combine TUKYSA with an ADC, trastuzumab emtansine or T-DM1, and improved PFS in the

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second-line-plus metastatic setting. A final OS readout is anticipated sometime in the future, late '27 or early '28 to complete the data set for that trial, but the results were very encouraging.

So moving now to the HER2CLIMB-05 trial. This is where we seek to establish this new frontline maintenance approach or backbone for HER2-positive metastatic breast cancer. And this trial has evaluated TUKYSA plus pertuzumab and trastuzumab versus pertuzumab and trastuzumab, so it's add-on design after the completion of induction therapy, and we anticipate this readout in 2025. Finally, we aim to advance TUKYSA in combination with T-DM1 into the curative-intent post-neoadjuvant setting. And this is being studied through a U.S. cooperative group the alliance is running the trial, and that has an anticipated readout in 2028.

So as you can appreciate, we are meaningfully expanding our portfolio in breast cancer, 8 compounds having active development programs, 7 ongoing Phase 3 studies. We anticipate multiple key catalysts through the end of this year and into the first half of '25 with the potential for continuous readouts and additional data-driven opportunities spanning over the next 5 years. In the near term, we have the 2 Phase 3 starts for atirmociclib, which I walked you through, with our second-line study in combination with fulvestrant already enrolling and our frontline study in combination with an AI initiating in the second half of this year.

We also look forward to readouts for IBRANCE in the HER2-positive setting and for vepdegestrant as monotherapy. And in the second half of '25, we expect to read out from TUKYSA, the HER2CLIMB-05 trial. And pending data from our ongoing combination studies with vepdegestrant, we will potentially initiate a Phase 3 frontline study of the 2 novel molecules together such as vepdegestrant plus atirmociclib. Longer term, we anticipate readouts from additional registrational trials for TUKYSA, the frontline study for vepdegestrant plus either atirmociclib or IBRANCE and our 2 atirmociclib trials.

Finally, we are excited by numerous opportunities across our expanding breast cancer portfolio, including the early-stage clinical molecules that you heard about today. With our innovative pipeline, which spans many segments of breast cancer, we believe we are well positioned to reach a significant portion of the over 200,000 addressable patients in the U.S. in the next decade.

So thank you, and I'll turn it now back to Chris to discuss our plans in hematology-oncology.

(presentation)

Chris Boshoff ***Pfizer Inc. - Executive VP & Chief Oncology Officer***

Thank you. I'm now going to walk you through our hematology-oncology portfolio, including our significant opportunity with ELREXFIO, our BCMA bispecific antibody for multiple myeloma. Pfizer has significant experience in hematology-oncology with 9 approved medicines that reach over 22,000 patients with our combined portfolio in 2023 alone. These medicines span all 3 core modalities to treat various types of blood cancers, including multiple myeloma, chronic and acute leukemia as well as lymphoma.

With the addition of ADCETRIS, we now have an established blockbuster in our portfolio that is the foundation of care for CD-30 expressing lymphomas. ADCETRIS is a first-in-class ADC that first received FDA approval in 2011. Today, it is approved in a total of 7 indications to treat Hodgkin's disease and certain T-cell lymphomas in various settings, including as frontline therapy for both adult and pediatric patients.

We have a substantial near- and long-term growth opportunity with our hematology-oncology portfolio, most notably with ELREXFIO, our BCMA CD3-directed bispecific antibody. We received the first FDA approval for ELREXFIO in 2023 in relapsed or refractory multiple myeloma, and we have a comprehensive clinical development program ongoing to potentially expand its use across treatment settings.

Our vision for ELREXFIO will be the main subject of this presentation today. We are also exploring various novel and differentiated molecules in our clinical pipeline across modalities, including a potential next-generation ADCETRIS. And Jeff Settleman will cover some of these during his presentation. With the addition of the Seagen hematology team, we have substantially strengthened our capabilities with expanded experience and scale to benefit our medical and commercial efforts with ELREXFIO now and in the future.

As I noted, ADCETRIS has been on the market for more than 12 years, and it has been prescribed to over 55,000 patients in the United

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States. Our colleagues from legacy Seagen have built deep relationships with the hematology-oncology community across stakeholders, including physicians, patients, and patient advocacy groups. As part of the integration planning, we have cross-trained our customer field force from both companies. We have now doubled the number of commercial sales team promoting ELREXFIO in the field.

Importantly, we also now have integrated field medical teams delivering world-class health care provider scientific engagement both in academic and in the community settings. This puts us in a solid position to broaden our presence with hem-onc customers as we launch the potential larger indications for ELREXFIO, pending clinical trial and regulatory success.

Now turning our attention to our opportunity with ELREXFIO in multiple myeloma. There were approximately 35,000 new cases of multiple myeloma in the U.S. in 2023 and approximately 13,000 deaths. Patients often cycle through several rounds of therapy. And after each relapse, there is a higher risk of treatment resistance, shorter remission and shorter duration of response. That's why several companies are actively exploring many types of interventions and novelties for multiple myeloma. The global market size is estimated today at $29 billion and forecasted to grow to $44 billion by 2030.

Now let me walk you why we believe ELREXFIO is well positioned to become a treatment of choice for multiple myeloma across different (inaudible) based on the results so far, ELREXFIO has a very promising efficacy profile with strong objective responses and complete remission rates and a remarkably long median progression-free survival in a highly refractory patient population with a median of 5 prior lines of therapy. Importantly, as a subcutaneous option, it has several convenience factors, flat non-weight-based dosing and a flexible dosing regimen. ELREXFIO is the only BCMA bispecific with the ability to switch from weekly to bi-weekly as early as 24 weeks.

It also has a tolerable safety profile with limited hospitalization during the step-up dosing period to manage the risk of cytokine release syndrome. In line with the data, the U.S. label recommends that patients be hospitalized for 48 hours following the first step-up dose and 24 hours following the second step-up dose. This is half the total step-up hospitalization time recommended in the U.S. label for other approved BCMA bispecific antibodies.

Now let me go into more detail about the efficacy data. The first pivotal trial for ELREXFIO is MagnetisMM-3, a Phase 2 study in patients whose disease has relapsed or is refractory to three primary classes of existing treatments. This is a broad, heavily pre-treated patient population. In particular, I want to call your attention to the table. A high percentage of patients -- 97% - enrolled in MagnetisMM-3 were considered triple-class refractory. Also approximately 40% of patients were penta-drug refractory receiving up to 6 lines of previous therapy.

In addition, MagnetisMM-3 included a significantly higher number of patients with extramedullary disease, which is also an unfavorable prognostic marker. This is a very advanced patient population with characteristics associated with poorer outcomes. Despite this, ELREXFIO has shown the longest reported median progression-free survival at 17.2 months for this setting. Also of note, the ELREXFIO curve appears to have plateaued around the top median. While we can't draw conclusions with cross-draw comparisons, we are very encouraged by these data.

If we now focus in on duration of responses with ELREXFIO, we can also see the plateau of the Kaplan-Meier curves. On the left is the overall responding population where the median duration of response has not yet been reached. On the right is the striking durability of response for the almost 40% of patients who achieved a complete remission or better. Median duration of response has still not yet been reached at 18 months follow -- again, you can see the plateauing of the curves. We believe these are truly remarkable outcomes in this setting. These are very deep and durable responses. And we now have patients who have been treated with ELREXFIO for more than 3 years in this very late-line setting.

We also plan to update these data, including overall survival data from the MagnetisMM-3 study later in 2024, which we believe has the potential to solidify the compelling clinical benefit of ELREXFIO. We expect these data to only get stronger as we move to earlier lines of therapy. We have designed a well thought out development program to offer an ELREXFIO-based treatment regimen across all lines of therapy. And over time, we anticipate expanding to significantly larger eligible patient populations with larger duration -- longer durations of therapy.

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In the relapsed/refractory setting, the eligible patient population is 18,000 in the U.S. We have 2 studies ongoing here: MagnetisMM-5 and MagnetisMM-32. MagnetisMM-5 has been designed to evaluate the superiority over a daratumumab-based regimen in the [second] line-plus setting. This study has completed enrollment, and we anticipate results in the first part of 2025. MagnetisMM-32 is a trial designed to address unmet needs in the rapidly changing landscape to position ELREXFIO as the new standard of care for patients with disease relapsing on anti-CD38 and immunomodulatory therapy in the frontline setting.

Our goal here is to generate data establishing ELREXFIO as the go-to second-line choice in the relapsed/refractory setting in the medium term. In parallel, we're evaluating ELREXFIO in the newly diagnosed setting, where the patient population significantly expands to 31,000 in the U.S. We have 2 ongoing studies here, the MagnetisMM-7 trial as a post-transplant maintenance option and the MagnetisMM-6 trial in transplant-ineligible patients comparing ELREXFIO to the current standard of care.

These studies are recruiting well with results expected in 2027, 2028 time frame. Altogether, these 4 studies are enrolling more than 2,000 patients over the next few years, which speaks to the strength of the data we have to date and the strength of the data generated with ELREXFIO.

In summary, we are excited by the potential for ELREXFIO to reach a rapidly expanding number of patients globally, subject to approval and positive readouts of ongoing studies. We are really encouraged by the data generated so far with a remarkable long median PFS and a deep and durable responses in the very late-line setting.

There are multiple catalysts anticipated over the next 2 years, including data from the MagnetisMM-5 and MagnetisMM-32 studies and the second-line-plus setting. And longer term, we anticipate results from the additional pivotal trials to potentially move into the frontline setting. In addition to these pivotal programs, we also are investigating potentially differentiated novel combination approaches with ELREXFIO as well as the early disease setting with a Phase 2 study ongoing in smoldering multiple myeloma collaborating with the European Myeloma Network.

With our ongoing Phase 3 program, we are well positioned for ELREXFIO to reach a significant portion of the over 50,000 addressable patients in the U.S. during the next decade. We also have additional candidates in development in the early pipeline. We are planning to start Phase 1 and 2 studies with additional mechanisms of action for various types of blood cancers through 2025 and anticipate providing more updates of these in the next 1 or 2 years.

Thank you. And now I'm going to switch gears to our next-generation opportunity presentation by Jeff Settleman.

I'd like to introduce Jeff Settleman, our Chief Scientific Officer. Jeff leads all oncology research from the beginning stages of discovery to IND-ready programs. Jeff is an internationally recognized leader in molecular-targeted cancer therapeutics, in the epigenetics of cancer drug resistance, and personalized cancer medicine. He held numerous notable positions in both academic research and drug discovery before joining the Pfizer team. Prior to his current role, Jeff served as Head of Oncology Research at Calico Life Sciences. And prior to Calico, he led Discovery Oncology at Genentech.

I'll now turn it over to Jeff. Thank you.

Jeffrey Settleman ***Pfizer Inc. - Chief Scientific Officer, Pfizer Oncology***

Thank you, Chris. So thank you all for joining us today. You've now heard about several of our approved cancer medicines and several advanced clinical-stage programs. And now I'm excited to discuss our current areas of research focus and a few potentially transformative early-stage programs.

I'll start with this slide, which simply highlights our 2 major R&D hubs for oncology. Both are on the West Coast. One is the newly acquired site in Bothell, Washington, north of Seattle, formerly a Seagen site. And the other is in La Jolla, where we recently made the decision to move to a brand-new state-of-the-art facility pictured here. It's located a few minutes from our current site. And the vast majority of our lab-based oncology research activities will take place at these 2 sites. And we're already seeing how having our 2 main research sites in the same time zone can actually go a long way toward facilitating communication and collaboration.

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So with the acquisition of Seagen, we see many opportunities to combine our scientific expertise, our technologies and our molecules to enhance the discovery and development of the next generation of cancer therapies. And here, we're highlighting 3 especially important opportunities that we see for scientific synergy. First, we'll be leveraging Pfizer's protein engineering and antibody design capabilities to enhance the legacy Seagen's ADC technology to deliver next-generation antibody conjugates with innovative new features. We'll also be incorporating Pfizer's deep expertise in small molecule drug discovery into legacy Seagen's ADC platform to advance next-generation ADCs with differentiated payloads with new mechanisms of action. And lastly, we'll be combining legacy Seagen and Pfizer molecules from our now substantially expanded aggregate portfolio to enable new mechanistic synergies and potentially reach many more patients.

And with our expanded portfolio, we have new opportunities to attack tumors from multiple angles and to extend the reach of our science in many indications. The portfolio currently features 3 modalities enabled by deep technical expertise and experience. Those 3 core modalities include the ADCs, as you've heard about, the IO biologics, including bispecific antibodies and the small molecules.

Our ADC portfolio grew substantially, of course, with the acquisition of Seagen, and this platform has already successfully enabled 6 of the 11 FDA-approved ADCs. And the next-generation platform is now aimed at novel targets and improved and differentiated payloads. Several of them are listed on the slide here, and I'll focus on the ones in blue today.

Moving to the IO biologics. You heard about ELREXFIO from Chris just now, and we continue to leverage our combined expertise in protein engineering and antibody design as well as immuno-oncology to develop next-generation biologics.

And in the small molecule space, Pfizer has a long history of deploying world-class structure-guided drug discovery and medicinal chemistry expertise to deliver innovative, best-in-class and first-in-class small molecule cancer medicines. Targets for some of these are listed here on the slide, and they include some approved medicines, clinical candidates, and there's one preclinical program that's expected to enter clinical development very soon. I'll be discussing the ones highlighted in blue here.

And all of these were discovered or enabled by work done in Pfizer research labs. In addition to the clinical-stage programs, we have a discovery and preclinical stage pipeline with 63 programs currently with opportunities for rational combination therapies with the potential to change treatment paradigms in many indications.

Now I'll spend a few minutes on each of these 3 modalities, starting with next-generation ADCs. So with this time line of ADC development, it's easy to see that Pfizer now has a substantial footprint on the current landscape of ADCs. Currently, there are 11 FDA-approved ADCs. Five are Pfizer products. Two others employ licensed Seagen technology, and one additional Pfizer product listed here, disitamab vedotin, which you heard about earlier, is approved in China. And now we're looking to build on that success with next-generation ADC technology, which I'll describe.

So to further strengthen our leadership in the ADC space, we're advancing our pipeline with novel targets and diversified linkers and payloads. So starting on the left, I've listed 4 of the FDA-approved vedotin ADCs to highlight the strength of the vedotin linker payload. And this is why we're still developing vedotin ADCs, as you've heard.

Moving to the right. We've listed clinical-stage vedotin ADCs. You heard about the encouraging efficacy already for 3 of these, and I'll have more to say about the felmetatug or the B7-H4 ADC. As Megan noted, the vedotin ADCs can elicit an especially immunogenic cell death with the potential for robust combination efficacy with immune checkpoint inhibition. This was very nicely exemplified by the PADCEV-KEYTRUDA combination clinical experience, as Tom described earlier, with synergistic efficacy seen in urothelial cancer.

And then moving again to the right. We also recognize the important opportunity to complement the vedotin technology with some novel differentiated linkers and payloads. Here, we've listed several programs that deploy a novel very potent topoisomerase inhibitor payload, and I'll describe 2 of those shortly.

Moving again to the right. We're also developing next-generation auristatin payloads with potentially improved tolerability. And then

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moving all the way to the right, you can see we're describing some discovery and preclinical stage programs that employ payloads with distinct mechanisms of action, for example, immune agonists, and I'll discuss the first one listed there.

And then we're also pursuing protein degraders as antibody conjugates, both with internal capabilities and through a research collaboration with Nurix, a leading protein degrader company. And we're especially enthusiastic about this protein degrader class of payloads. And we're pursuing various novel cytotoxic payloads with some very highly differentiated mechanisms of action. So with most of these programs now either in the clinic or moving to the clinic this year, we believe we're now uniquely positioned to bring forward the most extensive ADC portfolio in the industry, which includes a variety of novel and differentiated programs.

Now I'll go deeper on a few of the next-generation ADC programs, and I'll start with CEACAM5C, which includes a potential best-in-class topoisomerase 1 inhibitor payload. This program is partnered with Sanofi, and it employs their CEACAM5-directed antibody tusamitamab.

So CEACAM5 is a protein expressed on the surface of many solid tumors at relatively high levels. I've listed some of the tumor types here. It has a drug antibody ratio of 8, this particular ADC. And we're seeing some very remarkable activity in preclinical models shown here on a panel of patient-derived xenografts from both lung and colorectal cancer, where we see very strong robust tumor growth inhibition across many models. And this is notably following a single administered dose of the ADC. So it's a very promising program. The Phase I dose escalation is now underway. Clinical proof of concept is planned initially in colorectal cancer with an opportunity to expand to additional solid tumor types.

On the next slide, I just showed you data that highlights the robust antitumor activity that our TOPO1 inhibitor can deliver as a payload in preclinical models. Now here, we're directly comparing our TOPO1 inhibitor payload to the deruxtecan TOPO1 inhibitor in preclinical tumor models. So there are 3 examples shown here with 3 different ADC antibodies. And what you can see in each case, where we've taken each antibody and conjugated it either to our TOPO1, our novel payload or to deruxtecan labeled DXd here. The TOPO1 inhibitor, ours, is in the dark blue curve. And in all 3 cases, you can see evidence of a superior antitumor control with the matched antibody that includes the TOPO1 novel inhibitor.

So we're very optimistic about the potential for this new TOPO1 inhibitor as a differentiated ADC payload that drives robust antitumor activity across many models. And we expect to have up to 4 ADCs with this new payload in the clinic by the end of next year. And one of those programs is described here, 35C. It's a next-generation CD30-targeted ADC with the potential for an improved therapeutic index versus brentuximab vedotin, also known as BV or ADCETRIS. This is our approved ADC targeting CD30. And this also includes our novel TOPO1 drug linker. And in nonclinical lymphoma models, we've observed dose-dependent potent antitumor activity, as shown on the upper graph in a Hodgkin's lymphoma model.

And then in a tumor model below that, that's resistant to ADCETRIS due to increased drug efflux activity. This 35C ADC shows very robust antitumor activity, suggesting the potential to overcome clinical resistance to ADCETRIS that's associated with drug efflux, which could be very impactful for patients. We've also seen evidence of improved tolerability in preclinical models, so there's no observed hematologic toxicities at the highest non-severely toxic dose and no pulmonary toxicity seen at any tested dose. So we're excited about this program, which is expected to enter Phase I clinical development this year.

And now I want to touch on our PDL1iT program, which involves a unique antibody conjugate approach to promoting antitumor immunity. So this molecule, which is illustrated here, is designed to deliver a potent immune-stimulating TLR7 agonist to the tumor microenvironment. Last year at AACR, we described a macrophage and a targeted antibody conjugated to this TLR7 agonist, which is shown on the upper right, that it induces much lower levels of systemic circulating cytokines such as IL-6, which is shown here, when compared with administration of the unconjugated TLR7 agonist. And when we conjugate this TLR7 agonist to a PD-L1 antibody, we see potent single-agent tumor regression on the bottom graph, and this is maintained even following tumor rechallenge.

So together, these data suggest that this antibody-conjugated TLR7 agonist has the potential to deliver a very effective dose of TLR7 agonism to the tumor microenvironment but without the immune toxicity that one would expect with systemic administration of a TLR7 agonist. And this antibody conjugate uses that same proprietary PD-L1 antibody that Megan discussed earlier, which was designed for

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enhanced internalization, has an optimized drug linker and a payload and an antibody format that's been optimized as well. So we have very high hopes for this new immune-stimulating antibody conjugate. The IND is expected this year. And our target indications include non-small cell lung cancer, head and neck squamous cell cancer and melanoma.

So here on the next slide, we're highlighting early Phase 1 data not previously shared with one of our investigational vedotin ADCs, felmetatug. The ADC targets B7-H4, which is highly expressed in many tumor types, especially on breast, endometrial, and ovarian cancers, with much lower levels on normal tissues and immune cells. And we're seeing in these waterfall plots to the right very encouraging efficacy in our Phase I dose escalation study from cohorts of triple-negative breast cancer and HER-positive HER2-negative breast cancer.

And as shown in the table below, there are early signs that B7-H4 levels could be a potential biomarker with an expression response association in triple-negative breast cancer such that the overall response rate in allcomers was 21.4%, but it increased to 38% in patients with more than 50% of tumor cells expressing B7-H4. It's an early signal. It will require more data before we can establish clearly whether this could be a biomarker used to stratify patients for treatment. And while we're only showing clinical activity here in breast cancer, we're also exploring endometrial and ovarian cancers, and we're very encouraged by early signals in all of these indications.

So now I will pivot from our ADCs to our immuno-oncology biologics, which includes bispecific antibodies as well as other antibody-based programs. So with the acquisition of Seagen, we are significantly expanding our immuno-oncology biologics pipeline with a variety of innovative new programs, 2 of which are shown here. One of these involves an immune-engager bispecific antibody that was exclusively licensed from Lava Therapeutics. It's designed to redirect so-called gamma delta T cells to tumor cells to promote tumor cell killing, and I'll go deeper into that program in a minute. And then on the right is a second program that originates from our research labs in La Jolla and involves agonizing the lymphotoxin beta receptor to promote so-called tertiary lymphoid structures and tumors, and I'll explain the therapeutic hypothesis in a moment.

So on the next slide is a description of our EGFRd2 bispecific program from Lava. It's a potential first-in-class gamma delta T cell redirecting treatment for solid tumors. One arm of this bispecific antibody binds to EGFR on the surface of tumor cells, and the other arm binds to the gamma delta class of T cells and activates and delivers those T cells to EGFR-expressing tumor cells, resulting in the innate immune response.

And on the right, I'm showing survival curves from our preclinical xenograft model derived from a KRAS-mutant colorectal cancer. And here are the bispecific antibody at 2 tested doses extends survival of tumor-bearing animals, so providing some nice preclinical proof of concept for this novel modality. And importantly, in exploratory preclinical safety studies with a surrogate antibody, we saw no cytokine release syndrome, suggesting the potential for less immune toxicity than we've observed with other types of T cell redirecting immune engager antibodies. The Phase I dose escalation study is now underway, and the key potential indications include colorectal cancer, non-small cell lung cancer and head and neck squamous cell cancer.

This next program involves a very novel therapeutic approach in which we've discovered an agonist antibody that engages the lymphotoxin beta receptor to induce so-called tertiary lymphoid structures or TLSs. These are immune cell aggregates resembling secondary lymphoid organs. And they've been reported in several tumor types, and there are accumulating reports that show an association between TLS formation and maturation and response to anti-PD-1 therapy. And an example of that is shown in the graphic on the left. It's from a Nature paper which suggested that in melanoma patients treated with an anti-PD-1 antibody, that their overall survival was significantly increased as a function of having more mature TLSs in their tumors.

So the hypothesis is that promoting these TLSs could have therapeutic benefit for some solid tumors, especially when combined with checkpoint inhibition. So to activate the lymphotoxin beta receptor, we discovered a potent antibody agonist, pictured in the middle, which involves an innovative tetravalent antibody format that activates the receptor, leading to expression of multiple immune cell recruiting chemokines.

And when we treat tumor-bearing animals for several weeks with this agonist antibody, we see evidence of treatment-induced TLSs, as

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shown on the right, in these pre- and post-treatment tumor tissue sections stained for markers of TLS structures, showing that this antibody has the potential to induce the formation or maturation of TLSs at least in a preclinical tumor model. So this unique and very exciting and differentiated IO program is expected to enter the clinic in the next few months.

Now I'll move on to the last of our 3 core modalities, our next-generation small molecule inhibitors. So I'll start with our first-in-class CDK2 selective small molecule inhibitor, which is designed to prevent or overcome resistance to the widely used CDK4/6 inhibitors in ER-positive breast cancer. And we see this molecule as a potentially important combination partner for our CDK4 selective inhibitor, which Roger described earlier.

Now CDK2 and CDK4, as shown in the schematic on the left, can cooperate to regulate some understood key cell cycle checkpoints, suggesting some potential functional redundancy between CDK2 and 4. And consistent with that hypothesis in preclinical and clinical studies, we've seen evidence that activation of CDK2 may play a significant role in resistance to CDK4/6 inhibitors in a subset of breast cancers. So we've hypothesized that combining CDK2 plus CDK4 inhibitors could deliver synergistic benefit and potentially prevent or overcome resistance to the standard of care treatment.

Here are some supportive nonclinical data in the form of xenograft studies from 2 different models. The 2 on the left are from a CDK4/6-naive model and on the right are from a palbociclib-resistant PDX model, patient-derived xenograft model. There are monotherapy controls, but also combination treatment arms in each case, either CDK2 plus palbociclib on the left, followed by CDK2 plus CDK4 inhibitor, the same in both pairs.

Two key takeaways here. We see clear mechanistic synergy with the CDK2 plus 4 combination. So the second and fourth graphs. The red -- the purple curves are the 2 plus 4 treatment. We also see that CDK2 does better when combined with CDK4 than with palbo, and CDK2 plus palbo that is in the red on the first and third graphs.

So this is not surprisingly. We know, as you heard, that CDK4, our CDK4 inhibitor is predicted to cover CDK4 much more effectively than palbociclib can, and also spares CDK6, and therefore, has the improved safety profile that you saw earlier.

Now in Phase 1, we've seen monotherapy efficacy with confirmed PRs in heavily pretreated ER-positive, HER2-negative metastatic breast cancer patients. This was reported at ASCO. And we have multiple ongoing dose expansion cohorts underway, CDK2 inhibitor plus endocrine therapy and then CDK2 inhibitor plus endocrine therapy plus our CDK4 inhibitor. So we're excited to build on the encouraging clinical efficacy that Roger described for our CDK4 selective inhibitor, with this rational scientifically-understood combination approach.

Next, I want to discuss our next-generation brain-penetrant mutant BRAF inhibitor, which is designed to address some of the limitations of currently approved BRAF inhibitors. So to remind you, on the left, 39% of melanoma patients harbor BRAF mutations, and the activity profile of our inhibitor preclinically predicts that it should inhibit several forms of mutant BRAF proteins. There's the Class I that are most commonly seen on the top there, and as well as Class II and Class III, which are not addressed with current BRAF inhibitors. We predict that our new BRAF inhibitor will cover these mutations as well as mutations that importantly arise on treatment with current BRAF inhibitors and lead to the resistance associated with mechanism shown below, such as BRAF splice variants and NRAS mutations.

And importantly, these second -- these resistance mutations, which appear in the second row here, can potentially be addressed with our novel inhibitor. In fact, in nonclinical models, our molecule displays activity against several of these mechanisms shown here, including the BRAF splice variants and the activating NRAS mutations.

And then on the right are some nonclinical experimental data showing superior antitumor control in a melanoma xenograft with our -- that has a BRAF Class I mutation when comparing our new BRAF inhibitor, brain-penetrant BRAF inhibitor with a variety of things here, but most notably the encorafenib-binimetinib combination standard of care doublet, which is the purple hash lines on the upper graph versus on the right in blue, the single-agent treatment with this novel BRAF inhibitor. So a very impressive comparative preclinical data.

And then below that, as a brain-penetrant BRAF inhibitor, this molecule demonstrates superior antitumor control in an intracranial xenograft model when compared to the encorafenib-binimetinib doublet, which is on the left. You can see on the right, single-agent

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treatment with this new BRAF inhibitor, very remarkable antitumor activity in this intracranial model.

This is underway. There's an ongoing Phase I study, where multiple confirmed responses in RAF inhibitor refractory patients have been observed both systemically and intracranially. These promising new nonclinical and clinical data will be presented at the AACR meeting in April.

So lastly, I'll discuss our KAT6 inhibitor program. So KAT6 is an epigenetic regulatory enzyme, a histone acetyltransferase. The KAT6 proteins are part of a gene regulatory complex that affects the expression of genes involved in estrogen signaling, cell cycle signaling, oncogenic signaling. And we've discovered a very potent and selective first-in-class small molecule inhibitor of KAT6.

In preclinical models, this molecule can potently repress the expression of the estrogen receptor that's shown in the upper right. There's brown immunohistochemistry staining from an estrogen receptor-positive xenograft of a breast cancer. On the right, following treatment, 3 mg per kilogram, we see very strong repression of -- expression of the estrogen receptor.

And then below that, we see dose-dependent tumor growth inhibition in a preclinical xenograft model derived from an ER-positive breast cancer patient who had been previously treated with palbociclib plus letrozole where we see complete regression at 3 milligrams per kilogram of daily treatment. So a very potent molecule.

And in our Phase I study that's underway, we previously reported several confirmed responses during dose escalation. And now we're showing for the first time, some very promising data from an expansion cohort of metastatic ER-positive, HER2-negative breast cancer patients who had all progressed after CDK4/6 inhibitor plus endocrine therapy.

43 patients in this cohort, all heavily pretreated, as many as 6 prior lines of treatment. They were treated with 5 milligrams once per day of the KAT6 inhibitor plus fulvestrant. And we've seen very encouraging and durable clinical benefit: confirmed overall response rate in this heavily-pretreated patient population of 27.9%; and importantly, a median PFS of 7.5 months, which is 5 months improvement over fulvestrant alone in the semi setting.

It's a generally well-tolerated treatment, only 7% discontinuation rate due to AEs. Most frequently, we saw low-grade dysgeusia, a change in taste. And we're now optimizing the dose and schedule to improve on this dysgeusia, and then we'll decide how best to advance this program, which is highly differentiated, but very promising, into late-stage clinical development.

And now in the final slide, we listed here many of our promising early clinical and preclinical programs, just to give you a broader perspective on our early oncology pipeline. Notably, we've only listed selected preclinical stage programs here. A few of these haven't been disclosed previously, and we have several others that we expect to be able to disclose in the near future. We also have a large number of discovery stage programs in our newly expanded oncology pipeline that aren't shown here. And so with this diversity and scope of innovative new molecules, we're very enthusiastic about the opportunity for our early pipeline to deliver multiple potentially transformative new medicines across many indications.

So thank you. And I'd now like to turn it back to Chris.

Chris Boshoff ***Pfizer Inc. - Executive VP & Chief Oncology Officer***

Thank you, Jeff. You've heard a lot about our vision and about our portfolio. I would now like to ask Suneet Varma, to come up and present to you how we will potentially bring these great and breakthrough therapies to patients commercially.

Suneet has been a commercial leader at Pfizer, and before that, at Wyeth, for a total of nearly 30 years. He held a number of leadership positions before joining oncology, including Global President of Rare Disease and also Global President of the Hospital Unit. So thank you, Suneet.

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Suneet Varma ***Pfizer Inc. - Commercial President, Pfizer Oncology***

Okay. Everybody with us still? Good, good, good. I'm the last session before we go to the second Q&A panel.

Thank you, Chris, for that warm introduction. And let me begin by talking about the patients that we serve. Last year, we reached over 2 million cancer patients across Pfizer's innovative oncology portfolio and our sterile injectables portfolio, including the cytotoxics in our hospital unit.

Of those 2-plus million patients, 1 million were treated through our core innovative oncology unit, just to put that number in perspective. And as you all know, Pfizer's greater purpose is breakthroughs that change patients' lives. And simply put, our financial performance is a natural byproduct of the patients we plan to serve. And I'm pleased to say that since close of the Seagen transaction, as you all know, was in mid-December, we have integrated our 2 companies fully into one new Pfizer Oncology commercial organization, which is now operational, fully operational.

And as you also know, but I'll reinforce what Chris had said earlier, we have taken a best-of-both approach to design our organization, to select the talent at the leadership level and throughout, and also to preserve key capabilities and enhanced capabilities in several cases. Our commercial workforce is now a ratio of 60-40, legacy Pfizer, legacy Seagen, with a bicoastal presence and innovative sites across the United States. And as Chris mentioned, we have a presence in over 100 countries, which I will talk about later.

Further, we have organized our sales and marketing teams by tumor type. And this really allows us to focus sharply on each vertical and maximize our collective expertise, our relationships and our reach. A perfect example of this was our ability to quickly cross-train hundreds of IBRANCE and TUKYSA field-based colleagues, doubling our share of voice in HR-positive breast cancer.

So in other words, we took our IBRANCE reps from legacy Pfizer, train them on TUKYSA, boom, they're out in the market. We did the same with legacy Seagen, TUKYSA reps, train them on IBRANCE, boom, they're out in the market, 100% complete operational. And we did that in hematology as well.

As Chris showed earlier, we are proud of what we have achieved in Pfizer Oncology over the last 10 years, growing revenue at a rate twice that of the worldwide oncology pharmaceutical market. And this is owing obviously, the leading therapies that we have, including IBRANCE, which is a flagship and a pillar of our portfolio. And this means that as we go forward, we are going to build on that foundation of success. Success, which includes the talented colleagues with the deep knowledge and expertise in oncology, super important feature of being successful in a specialized area like oncology. But we also are going to take advantage of our vast geographic footprint and our commercial infrastructure to go to market and continue to drive leadership.

We expect continued strong sales and profit growth in oncology through the end of this decade, through 2030. And in the next few slides, I will show you the composition of what comprises that anticipated growth. And as you know, we do anticipate the U.S. patent expiry for IBRANCE and XTANDI in 2027, and so we factored that in. And despite those LOEs, as you've heard today, we still aim to double the number of patients treated through our innovative oncology medicines in our portfolio by 2030.

We believe this achievement will be possible due to the expected advancement of our innovative R&D pipeline. And by the way, that's why we spend a lot of time on that today, and that's why we're having this Innovation Day so we really have an appreciation of all the things that we're doing. And that is part of the story. However, we also have ongoing additional innovation for our currently approved products. So those 2 together are what drive our aspirations for 2030.

As you can see on this slide, as we look to 2030, we expect that 2/3 of our projected risk-adjusted revenue will come from new molecular entities, new indications for existing products and new data currently being generated by R&D. This will certainly impact from this year 2024 and beyond. That means our current in-line portfolio, which includes products on the market today and any new indications that were approved by the end of 2023, that represents the balance, 1/3 of our 2030 risk-adjusted revenue.

Likewise, as we grow, we are driving meaningful shifts in the makeup of our portfolio. While today small molecules comprise the vast

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majority of our commercial portfolio, by 2030, we plan to increasingly rely on revenues generated by complex biologics, including ADCs and bispecifics and some of the other products you heard about today in our pipeline.

Biologics represents a more durable revenue potential based on a number of factors, including differentiated access and affordability to the patient, IRA considerations and patent expiration time line, specifically exclusivities, which are statutory versus what is natural and hard-to-make complex biologics. This planned shift to biologics as the main source of revenue is expected to support the accelerated growth of both our top and bottom line.

When we look at our portfolio by tumor type, we also see other shifts. As you heard today, breast remains important, but it is expected to represent a smaller portion of our 2030 risk-adjusted revenue due to the expected loss of exclusivity for IBRANCE. This will be partially offset by our follow-on new assets in breast in the time frame that we're talking about.

Our GU portfolio, comprised of bladder and prostate cancer, is expected to become our largest franchise. This is driven by PADCEV, but it is also driven by our prostate cancer portfolio, especially in the U.S.

Earlier today, you also heard about hematology. This was previously more nascent within Pfizer. Long history, but a smaller franchise overall. This will become more prominent right now, starting with the addition of ADCETRIS and the expected growth of ELREXFIO through potential new data and new indications. And I should say those new indications will be in earlier lines of use, with larger patient populations, as Chris defined, and those larger patient populations and earlier use also lead to longer durations of therapy.

TC is our smallest indication. That's where we're starting. But what's coming is much bigger and better. Lastly, thoracic is anticipated to expand with breakthroughs in lung. And this has the potential to scale up and become its own stand-alone franchise at Pfizer in the future. So we are moving from relying heavily on breast cancer as the main source of revenues in '23, to a more risk-balanced portfolio in 2030.

Clearly, there's a lot to be excited about between now and 2030. That being said, we're highly focused on the here and now, especially our commercial organization, especially our medical and the rest of our go-to-market organization. We are focused on the here and now, especially launches that are virtually upon us.

In our near term, we look at a 3-year horizon. And let me highlight a few programs that have great potential to become significant growth drivers. For example, as you heard today, in breast, we believe vepdegestrant and atirmociclib have the potential to replace the current standards of care, respectively, for HR-positive breast cancer. This is, of course, subject to positive clinical readouts and regulatory approval.

In heme, we have a robust ongoing development program for ELREXFIO, which you heard about also earlier today. If successful, this will enable us to potentially reach a significant portion of over 50,000 addressable patients across the treatment spectrum for multiple myeloma in the U.S. alone, with the next potential jump up in eligibility coming from double-class exposed, or DCE, relapsed/refractory, which adds 18,000 eligible patients in the U.S., if approved. Today, DCE, with the fifth line plus in the U.S., is about 2,000 patients. So just to give you an order of magnitude, 2,000 to 18,000 add 33,000; 2,000 to 50,000 by the time you're done.

In prostate, the TALAPRO-3 study if successful, has the potential to move PARP inhibitors into earlier utilization in the patient journey, significantly expanding the reach of TALZENNA plus XTANDI.

And finally, in bladder cancer, we believe that disitamab vedotin and sasanlimab have the potential to further solidify our expected leadership in this tumor area and GU, subject to approval.

Beyond our strong and differentiated pipeline, we also have a healthy and vibrant in the line portfolio. This is that other 1/3, and that underpins our current and future opportunities. And in 2024, the year that we're in now, we expect our 25 medicines and biosimilars, we are focused on the top 10 priority brands that represent 80% -- nearly 80% of our revenue.

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And let me speak to about half a dozen or so of these top brands, just to give you a sense, like, let's say, some brief thumbnails of what's exciting us about that. So you can be excited about 2030. We're very excited about '24 to '26, the 3-year, but what are we talking about that we're excited about right now in this particular year?

Let me start with IBRANCE, which as I stated earlier, is a major contributor of our revenue, however, but faces ongoing challenges from competitive headwinds. We all know that. However, we continue to fortify the base with ongoing data, reinforcing the body of evidence and clinical value of IBRANCE. There are years of experience and hundreds of thousands of patients that have been treated out there. And we intend IBRANCE to remain a foundational pillar of our portfolio as our other products increase in prominence and increase in growth.

Our bladder cancer portfolio is anchored by PADCEV, what we believe is essentially the new standard of care in locally advanced or metastatic urothelial cancer. 2023 versus 2022, on the Seagen side, we saw more than 60-plus percent revenue growth year-over-year. And what particularly excites us is that 70% of that came from the community, something Chris touched upon earlier. We are poised to expand PADCEV's leadership in urothelial cancer, with potentially double the eligible patient population for the combination of PADCEV and KEYTRUDA as first-line therapy for locally advanced or metastatic urothelial cancer.

XTANDI. It is well established as the standard of care, and it is the branded market leader in prostate cancer. We are especially excited to expand the leadership of XTANDI following the approval late last year in patients with non-metastatic, castration-sensitive prostate cancer with biochemical recurrence at high risk for metastasis, representing a potential paradigm shift by offering patients a new treatment option in the earlier setting.

TALZENNA. We are encouraged by our results to date for TALZENNA, while -- where we have seen our U.S. sales rate double in the second half of 2023 versus what we had seen in the first half of 2023. And we're excited for the upcoming global launches where TALZENNA plus XTANDI has now received approval in several key markets, including in Europe, for use in metastatic castration-resistant prostate cancer patients, with or without HRR gene mutation. So essentially, as it was pointed out earlier, in Europe, in an all-comers population. We are also preparing for the potential launch in earlier metastatic castration-sensitive prostate cancer in 2026, if our TALAPRO-3 study is also successful.

For ELREXFIO, this is just the start of something great. It's a very good product, as you saw from Chris, and it is poised to potentially become a new standard of care in multiple myeloma. I am happy to report that since we shared, and this is pretty fresh, you all know this probably, our 17-plus month PFS data at ASH in mid-December, so that's pretty new to the marketplace. ELREXFIO utilization has meaningfully accelerated in the United States. And we're looking forward to sharing even more updated median overall survival data from the MagnetisMM-3 study later this year.

ADCETRIS has been remarkably resilient continuing to rally on its 6-year OS data and grow in 2023 even post SWOG. It remains the only innovative treatment for Hodgkin's disease with NCCN Category I preferred status for those aged 60 and under.

And we're also extremely pleased with the performance of LORBRENA, which continued its double-digit growth rate in 2023. Globally, last year, also more than 60-plus percent, same number pretty much as PADCEV on the Seagen side.

Looking ahead, we eagerly await potentially practice-changing data from the CROWN trial this year, which could demonstrate outcomes exceeding those historically reported in patients with non-small cell lung cancer harboring an ALK translocation.

As you can see from this slide, we have built a strong go-to-market engine to deliver on both our in-line and our pipeline aspirations, and we are preparing the market for all of these launches, NMEs, new indications, new data. We believe our significantly expanded scale, infrastructure and commercial and medical go-to-market capabilities position us for the success to which we aspire.

Our new U.S. customer-facing footprint is nearly triple that of legacy Seagen alone, and it is 50% larger than of legacy Pfizer alone. Actually, I just came back from the West Coast, we had our year-beginning meeting, which was the first combined sales and marketing meeting for both legacy Pfizer and legacy Seagen in the new Pfizer Oncology. And it was fantastic. Couldn't have hoped it could be any

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better. The oncology cultural match between the 2 companies is indistinguishable between the 2 organizations and everyone is extremely focused on this competitive advantage that we're creating.

Through our field colleague cross-training initiatives, we expect to see and are already seeing a significant increase in the share of voice and promotion for those select in-line products. And as we think about launch excellence and we plan to leverage Pfizer's global operations, we can commercialize new unpartnered products, like -- such as some of the ones you saw today, in 5x the number of countries that legacy Seagen could have done alone.

Of course, while we operate as an integrated oncology unit within Pfizer, we still have the benefit of a large-scale, let's say, access to platforms and capabilities across the broader Pfizer enterprise. And that is a big advantage for us to drive performance. For example, we have a new Chief Marketing Office, and this is focused on driving higher ROIs on our sales and marketing investments. It also has allowed us to add additional data analytic capacity: more products, more data, more analytics.

And in addition, we have a dedicated access and value only for oncology group and an integrated medical affairs organization that is a part of our Pfizer Oncology team. This allows close alignment between clinical development, medical affairs and commercial execution. So upstream R&D, downstream go-to-market in one place. All of these organizations, therefore, are able to scale and share capabilities and learnings in their respective communities of practice across the Pfizer enterprise.

In conclusion, to deliver on our bold vision and position us for continued success, the Pfizer Oncology commercial organization is laser focused on 3 core priorities or guiding principles, let's say. First and foremost is preserving our talent and enhancing our capabilities. With the combination of colleagues from legacy Pfizer and Seagen, we believe our oncology expertise is unmatched in the industry. And this is a case, clearly where 1 plus 1 equals more than 2. Next, we have to ensure business continuity and operate as a newly-integrated company, which we're already doing. And we're minimizing distractions and disruptions so that our colleagues can prioritize and deliver on the needs of patients and customers. And finally, we have an unwavering focus on elevating our go-to-market capability to capitalize on our multiple near-term commercial catalysts. Francesca has said something earlier today, which I always liked, which is a catalyst-rich time in our existence.

Thank you so much. And I'll now turn it over back to Chris for the second Q&A portion. Chris.

QUESTIONS AND ANSWERS

Chris Boshoff ***Pfizer Inc. - Executive VP & Chief Oncology Officer***

Thank you, Suneet. We'll now start our next Q&A session. A reminder to line up to ask questions in the room and to please introduce yourself. Questions can also be submitted online. Joining us for our second panel alongside our speakers is Akos Czibere. Akos is our Therapeutic Area Development Head for Hematology-Oncology; Scott Peterson, who's Head of ADC Discovery and Cancer Immunology; and Adam Schayowitz, who's our Head of Product Teams, Portfolio and Program Management for Pfizer Oncology. And back here is also Megan O'Meara joining us. So on this side.

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

First on the CDK4 and the PROTAC programs, you referenced some early-stage adjuvant efforts. But maybe can you talk a little bit about lessons for maybe approaching adjuvant differently than maybe you did in the past? And specifically, sort of what should investors take away around Pfizer's conviction and confidence to move -- to go forward with those studies in an environment where some of the existing agents are facing IRA or generic pressures? And then maybe just quickly on MagnetisMM-05. Can you help frame sort of your expectations for that dara-pom-dex arm? We've seen repeated myeloma studies, sort of have comparators create an evolving views on exactly what the standard of care is here?

Chris Boshoff ***Pfizer Inc. - Executive VP & Chief Oncology Officer***

Okay, very nice. So I'll start, and then I'm going to ask Roger and then Adam to address the adjuvant. The only thing I'll say, if we conduct any future adjuvant trial in breast cancer, Pfizer will be the sponsor. So we will not externalize the study. Roger?

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Roger Dansey ***Pfizer Inc. - Chief Development Officer, Pfizer Oncology***

It's a great question. And I agree with Chris, we need to be completely in control of the trials that we run so we have the best quality and flawless execution. With regard to how to get to an adjuvant stage, and there are 2 elements. Number one, there's the existing sort of later-phase trials that are running, that are basically -- will give us the confidence to move into that adjuvant area if they are positive. So that's one signal.

And the second is doing some of these window of opportunities or sort of the adjuvant exploratory trials, looking at readouts that are surrogates for outcomes later with an adjuvant approach. So I think we have a plan. We'll need more data. We'll need a little bit more confidence around the molecule, which is why we're not jumping in now. We need to do some exploratory work. But that's the vision for the molecule. There's no reason to believe that CDK4 works in the later stage would somehow not work in an adjuvant environment.

Chris Boshoff ***Pfizer Inc. - Executive VP & Chief Oncology Officer***

Adam?

Adam Schayowitz ***Pfizer Inc. - Head of Product Teams, Portfolio & Program Management, Pfizer Oncology***

Yes, I think that's well said, Roger. I mean the -- there is an interest in moving both atirmociclib and vepdeg the early breast cancer space. The question is based upon the data that we have and the data that we're generating when and how we do it, but I think it's well said by both of you.

Chris Boshoff ***Pfizer Inc. - Executive VP & Chief Oncology Officer***

Myeloma.

Roger Dansey ***Pfizer Inc. - Chief Development Officer, Pfizer Oncology***

The myeloma question was, what was it again? Do you remember the question? Repeat...

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

On the MagnetisMM-05 study, the evolving landscape and how we think ELREXFIO will fit into the landscape.

Chris Boshoff ***Pfizer Inc. - Executive VP & Chief Oncology Officer***

So the MagnetisMM-05 study is a 3-arm study, right? So it investigates ELREXFIO monotherapy then ELREXFIO in combination with daratumumab versus the current standard dara-pom-dex. That study has to be viewed together with the MagnetisMM-32 study, which is essentially testing ELREXFIO monotherapy versus other standard of care in a setting where patients already have received a CD38 antibody in a frontline setting, right?

So with these 2 studies, we're basically covering the entire second-line patient population irrespective of what patients receive in the frontline setting. So we'll have data in both treatment settings, even though the MagnetisMM-05 study does not require patients to be naive for CD38 therapy. We do know that physicians don't like using CD38 after CD38, which with the controller being a CD38-based regimen we expect that study to be mostly patients who have not received a CD38 therapy. And that's study is fully enrolled. We're waiting on events now.

Roger Dansey ***Pfizer Inc. - Chief Development Officer, Pfizer Oncology***

It's addressing both populations.

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

Terence from Morgan Stanley, maybe a 2-part on myeloma as well. What are you seeing out there commercially in terms of sequencing CAR-T versus bispecifics? You mentioned you're seeing an acceleration in post the ASH data that you guys presented, but maybe just what are you seeing out there? Again, any difference between community versus academic uptake in terms of ELREXFIO?

And then the second part relates to FDA. FDA's, I think, been talking about or thinking about MRD negativity as an endpoint in myeloma for a long time. We've heard about this. We haven't seen any action. But obviously, would help as you think about some of these earlier

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line trials that you guys are running in terms of an end point. So has there been any movement from FDA in terms of moving to an MRD-negative endpoint?

Chris Boshoff ***Pfizer Inc. - Executive VP & Chief Oncology Officer***

These are very good questions that we think of all the time as well. So I'll start and then ask Suneet and then Akos.

So we know that the BCMA CAR T is, for certain patients, transformative. But the CAR T therapies are still, as you all know, a niche opportunity, which is very complex to globalize for patients globally. Having said that, on CAR T cells, patients also progress, so there's certainly an opportunity in the future to see if you can sequence and potentially post-CAR T, use a bispecific antibody to maintain maintenance. And we're interested in that and looking at that as future opportunity. Suneet?

Suneet Varma ***Pfizer Inc. - Commercial President, Pfizer Oncology***

Yes. If I can add, Chris, and that's exactly right. I think what's interesting that we're seeing also, especially with regards to the community, is that bispecifics really have that wide, I don't want to say, accessibility only but availability versus CAR-T as well because there's supply constraints. I believe they'll ultimately be worked out if you wait, let's say, 2 years or 3 years or whatever frame you might be assuming.

But I think what's happening is that the bispecifics having as a class and opportunity to be more widely used in the community. And I think elra, not just because of its most recent efficacy data, which is quite compelling, but also because it's ready-to-use, off-the-shelf not weight-based. It's particularly inclined. And of course, it's lower hospitalization and initiation 48 hours, 24 hours and then 0 versus 48,48, 48 for some of the other products, is particularly well placed to be used in the community.

Look, we talked about PADCEV being used, 70% of its uses coming out of the community. I think we have something to learn when we brought Seagen and Pfizer together to make the new organization to say, we have a road map, let's say, to make sure that complex biologics can be used effectively beyond the academic centers. And I think as this class gets used, elra is going to be very well positioned for those kinds of expansions.

Chris Boshoff ***Pfizer Inc. - Executive VP & Chief Oncology Officer***

Thank you. And then minimum residual disease is an endpoint, which is yes.

Akos Czibere ***Pfizer Inc. - Therapeutic Area Development Head for Hematology-Oncology, Pfizer Oncology***

Something we await eagerly just like you and everyone else in the field, I think the discussions have been ongoing with the elra consortium. FDA, there's another workshop. I think it's later next month, with the IMS and the FDA, what -- this will be discussed. Again. I mean, as soon as we hear about it, you'll hear about it. So we don't have any insight scoop, but we're hoping that the field will move there eventually in the near term.

And we just -- I mean just on the AML side, we saw now from the European hub -- from EMA coming out with guidance that they're willing to consider MRD for AML. So I hope that will maybe also jump start the same compensation for myeloma again. So the field will move there. The question is just when.

Chris Boshoff ***Pfizer Inc. - Executive VP & Chief Oncology Officer***

But we are building MRD as a potential co-primary endpoint in some of our studies so that we can grab the opportunity if it's available. And especially also now the context of potentially project frontrunner with the FDA, there's a potential to use MRD in that setting.

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

Chris Schott at JPMorgan. Just first on the CDK4, I guess, do you feel you need to show head-to-head superiority against standard of care to really have an opportunity here? I know that's probably the hope here, but to the extent you just saw a directional positive data with a more tolerable profile. Is that still an attractive opportunity for the company? Just maybe some context for that.

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And just since, I guess, the first kind of big Oncology Day we've had post IRA. Would these development plans across your portfolio look different in a pre-IRA world? So are you thinking about how quickly you move into frontline and adjuvant settings differently than you might have thought of a year or 2 ago as you kind of consider this broad portfolio and how to develop it going forward?

Chris Boshoff ***Pfizer Inc. - Executive VP & Chief Oncology Officer***

Two very good questions. For the first one, I'll ask Roger then Adam on this, for abemaciclib, do we need to show superiority versus just show a better tolerable drug in the noninferiority setting registration strategy?

Roger Dansey ***Pfizer Inc. - Chief Development Officer, Pfizer Oncology***

Yes. To deliver on the value proposition, which is of best-in-class backbone, we would need to be superior. A trial design with superiority is much easier to conduct than a non-inferiority trial too. But we have to have conviction with the molecule. I think that late phase data is really impressive. 100% CDK4/6 exposed, nevertheless, we're getting meaningful response rate. So I think that part -- do you want to comment on the IRA? Would you...

Chris Boshoff ***Pfizer Inc. - Executive VP & Chief Oncology Officer***

I'll come back -- we'll do the IRA, second.

Roger Dansey ***Pfizer Inc. - Chief Development Officer, Pfizer Oncology***

Adam?

Adam Schayowitz ***Pfizer Inc. - Head of Product Teams, Portfolio & Program Management, Pfizer Oncology***

No, that's it. I agree. Absolutely.

Chris Boshoff ***Pfizer Inc. - Executive VP & Chief Oncology Officer***

Yes. So we are currently -- I mean for atirmociclib, the data -- because we've got a lot of data to compare against the previous CDK4/6 development. So currently, we -- this is highly encouraging. And tolerability, the fact that very -- hardly any patients have to stop therapy due to AEs. That's very, very encouraging to take it into a first-line strategy.

For the IRA, Roger can start, then Suneet.

Roger Dansey ***Pfizer Inc. - Chief Development Officer, Pfizer Oncology***

Yes, I think from a pure drug development hat perspective, going as fast as possible into all lines actually makes sense. It got nothing to do with the IRA. It's just let's -- if you believe in the molecule, let's test it at every place we can and move it forward fast. That's obviously the approach that's probably most IRA-friendly because you get to the biggest populations in the fastest possible time.

I think one of the concerns that I have personally is just the limitations around very small, the usual sort of more traditional ways got right at the end of the treatment spectrum, get a very late line population approved and then move up even if you're running in parallel, you start the clock very early just based on a small population. So I think that does have some influence about how we think about what to do and when to do it. But shifting to biologics-based platform is helpful to that respect.

Suneet Varma ***Pfizer Inc. - Commercial President, Pfizer Oncology***

Yes. Actually, that's where I was going to go. I think, look, when we build our cases and we look at the investment thesis for what we're going to achieve. We look at a lot of factors. And the IRA, of course, didn't exist.

So we would always look at the high impact to patients and how differentiated it's going to be in the marketplace. We would look at access and affordability, I think Medicare Part B even is more favorable to biologics. Or let's say, a medical benefit versus the pharmacy benefits we do in Part D. We look at LOEs, but I think with complex biologics, the statutory loss of exclusive or patent expiry is very different than the natural exclusivity you might have because it's difficult to make complex biologics even post statutory. So that, let's say, you hold on to that exclusivity naturally a little longer.

And then you put in IRA, to your point, and biologics have that 13-year versus the 9 year before you enter negotiation or price

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negotiations. So I think that all of that strengthens the case and that has driven us to be deliberate and intentional not just on our tumor types, but on the modalities that you heard about today, the ADCs as well as the bispecifics. But I think when it comes to indications within a product, Roger answered that very, very well.

Akash Tewari ***Jefferies LLC, Research Division - Equity Analyst***

Akash from Jefferies. So with the DDI between IBRANCE and vepdeg, I think initially it was thought to be [SOC]. I feel like it's more CDK4-related. Can you confirm whether you expect the DDI with your next-gen CDK4 selective and vepdeg? And if so, how does that kind of fit into your data-driven strategy about what you're going to see in first line and you're going to have that data this year?

And then maybe, Suneet, when you're talking about PADCEV, I mean, obviously, I rarely see a drug get approved within 2.8 months. Can you talk about how quickly do you think you're going to actually replace standard of care? And what do you think ultimate penetration rates will look like? Any early feedback from the launch would be very helpful.

Chris Boshoff ***Pfizer Inc. - Executive VP & Chief Oncology Officer***

So I'll start with the DDI with Adam, DDI for (inaudible). So I mean as you heard us and Arvinas has talked about before, right? I mean there is an interaction between vepdeg and between palbo is the basis for the combination program or the lead-in associated with VERITAC-3, right, where we're looking at different doses of palbo in combination with vepdeg.

To your question, no, we don't believe that there will be an interaction with atirmo and vepdeg, but that's why we're doing the experiment, right? That's why we're doing that Phase 1b study to see are they combinable at the 2 full doses, and you saw that in Roger's presentation earlier. So we don't anticipate any interaction. But as you can see from the presentation earlier this morning, the frontline strategy of the combination of 2 novel backbones of vepdeg as well as atirmociclib is really going to be based on a data-driven decision that's going to look at VERITAC-3, what it comes out from that program as well as the Phase Ib combination and then we'll bring forward the most appropriate phase or frontline strategy.

Suneet Varma ***Pfizer Inc. - Commercial President, Pfizer Oncology***

Yes. And with respect to PADCEV, I think you nailed it. It's exciting. It's transformative. I mean standing ovation at ESMO, which never happens and then that rapid approval. I think we're pulling through that rapidity in how we're going to market as well. You saw earlier I talked about the 60% growth rate plus that we saw in 2023.

And essentially, let's say, this opportunity allows us to double the patient populations that are eligible for the product. We're doubling overall survival. And so we are seeing a significant uptake in the product already through normal, let's say, education and awareness building around this great data and the use of the product. And of course, we're working to support it further with guideline changes, pathway additions as well as publications, all of which are happening in a similarly rapid time frame from what we just saw.

So therefore, the results that we would have expected are happening. And we're very excited about it. You have seen in my presentation, I used the word mega blockbuster for the potential of this. We don't usually comment on peak year sales, like specifically by product. But a blockbuster is typically $1 billion, and we consider mega to be $3-plus billion. And so we are very optimistic for the future of this product.

Akash Tewari ***Jefferies LLC, Research Division - Equity Analyst***

And just to put a finer point on that, is there any potential that the Seagen acquisition could become an accretive deal internally within Pfizer by 2025, given the uptake in the early approval we've seen with PADCEV?

Chris Boshoff ***Pfizer Inc. - Executive VP & Chief Oncology Officer***

I'm not going to provide that guide. It's like I'll be sitting next to you, but we'll go to this side.

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

Louise Chen from Cantor. Just curious, do you have any interest in CAR Ts and/or radiopharm? And then second question is, do you ever see CAR-T making any meaningful inroads into the community setting and why or why not?

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Chris Boshoff ***Pfizer Inc. - Executive VP & Chief Oncology Officer***

Yes. On the CAR T, so we've outlined our strategy and our focus. A reminder that we externalized the allogeneic approach for CAR Ts. We're still very much interested in allogeneic CAR T cells. So we're following very closely Allogene, the company, because we've got a significant stake in Allogene. That's a company we started by externalizing our own internal portfolio.

So off-the-shelf CAR T cells. Also the future, potentially, in vivo gene editing to deliver. That's long-term options for patients. But right now, for us, the focus is on these modalities not to internalize right now CAR Ts, potentially collaborate and sequence, yes. I think we can talk more on the...

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

No, no, no, I was just going to ask you about, what about radiopharmacy?

Chris Boshoff ***Pfizer Inc. - Executive VP & Chief Oncology Officer***

Oh radiopharmacy. So it's interesting there's now at least 4 or 5 of these using exactly the same target, but slightly different radiopharmaceutical -- radionucleotides. Data very similar, very suddenly crowded competitive space. There's obviously an opportunity with the ADC platform to use immune agonists, degraders and potentially radioisotopes to link to ADCs. But for us, it has to be differentiated, much more differentiated, what's currently out there with 4, 5 similar projects, especially around PSMI.

Thank you. Do you want to add to that anything, Scott. Radio?

Scott Peterson ***Pfizer Inc. - Head of ADC Discovery and Cancer Immunology, Pfizer Oncology***

I think radio ligands are fairly complicated. And at Seagen, that was something we steered clear of, and so we'll see where we go here at Pfizer.

Chris Boshoff ***Pfizer Inc. - Executive VP & Chief Oncology Officer***

And clearly, we're -- it's not easy to globalize either. It's not easy to globalize. But...

Trung Chuong Huynh ***UBS Investment Bank, Research Division - Analyst***

Trung Huynh, UBS. So on elra, I'm curious on your thoughts on using a bispecific after using CAR T and another -- or another bispecific if they fail there. Does that impact efficacy? And you touched upon physicians not favoring using Darzalex after Darzalex failure. Just what your thoughts on BCMA after using BCMA.

Chris Boshoff ***Pfizer Inc. - Executive VP & Chief Oncology Officer***

Yes. And I'll ask Akos to comment on that because we've got data, we've got data for our MM-3 study.

Akos Czibere ***Pfizer Inc. - Therapeutic Area Development Head for Hematology-Oncology, Pfizer Oncology***

Yes. We actually presented data on ELREXFIO after CAR T therapy at ASCO last year. There was ASCO, one of the 2 in our presentation. And we're still seeing very robust response rates there. That data, we've updated. Follow-up is currently prepared for publication. So hopefully, we'll have that out soon. But we see over 50% response rate in that population, with a median duration of response that was not reached at the time of presentation.

So BCMA bispecific after BCMA CAR-T works, right? We know that. We've seen real-world data from CAR-T after BCMA bispecific, less active as CAR T first, small data sets, still real world, not sure what to make of that. We haven't seen BCMA bispecific after BCMA bispecific, so I don't have any data on that. If you're switching the target like GPRC5D for example, unless we completely exhausted the T cells, it should work. But again, we only have limited data in the field, and we don't have any of our own data there.

Trung Chuong Huynh ***UBS Investment Bank, Research Division - Analyst***

Understood. And on VERITAC-2, just your confidence on the 2H data is an event-driven study there. So what's your confidence there? And also, what's your confidence in the wild-type group as well?

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Chris Boshoff ***Pfizer Inc. - Executive VP & Chief Oncology Officer***

So our confidence is quite high based on the data we've seen. But Adam, do you want to add on VERITAC-2 to for the all-comers versus the ESR1 mutated population? Our confidence -- and the study, by the way, is got co-primary. So it's got dual primaries. So we've got 2 shots on goal, et cetera.

Adam Schayowitz ***Pfizer Inc. - Head of Product Teams, Portfolio & Program Management, Pfizer Oncology***

Yes. Chris, it's well said. So the first part of the question, we're still tracking to the second half of the year, right? So that's what we've said publicly and that continues. The dual endpoint does help between the ESR1 mutant as well as the wild type. When you look at the early Phase 1 data, we have -- the confidence that we have is really based on the stronger response rate in the wild-type population compared to some of the others that are out there in the early Phase I versus the wild type -- I'm sorry, in the wild type versus the mutant. So we think there's an opportunity to win in both and that we can win in both, but we do have the backup strategy and then with the 2 co-primary endpoints for the mutant if it doesn't pan out.

Chris Boshoff ***Pfizer Inc. - Executive VP & Chief Oncology Officer***

We were very encouraged, obviously, by the over 11 months median PFS we've seen now with the combination with IBRANCE in a setting, we don't expect that. So it give us great confidence.

Vamil Kishore Divan ***Guggenheim Securities, LLC, Research Division - Research Analyst***

Vamil Divan from Guggenheim. So maybe 2 commercial sort of on the GU side. So one, I think, Suneet, you mentioned that it's about 70% of the use for PADCEV in the community setting. So one thing we've heard just talking to doctors is the toxicity there and making sure community docs are familiar with how to give this and don't run into issues that could limit the uptake over time. So can you just talk about sort of how the education has been just on neuropathy, any feedback from the launch would be helpful.

And then second, just in terms of your work around DV and PADCEV in bladder, kind of curious about just using both of those patients? Is that something could be used in the same patient? Is there any potential that you're sort of cannibalizing one by moving people to DV or going to muscle invasive as opposed to as metastatic disease. How does that sort of impact kind of the use of that sort of franchise overall in that population?

Chris Boshoff ***Pfizer Inc. - Executive VP & Chief Oncology Officer***

So for the first one, I'm going to ask Suneet; and then for the second part, I'll add something and then ask Roger to add. So Suneet, if you start with...

Suneet Varma ***Pfizer Inc. - Commercial President, Pfizer Oncology***

I can, and Roger probably can add something to the marketplace. I think that have a concerted effort around education when we go to market for commercial -- we're using our commercial and our medical resources, and therapy management is part of that. We have found that the profile that you described is both manageable and predictable. And I think that's something that's really resonated very well. It's not a new, let's say, NME, it's been out in the market for a couple of years now. And we're building upon, let's say, that foundation, especially as we expand and deepen in the community and, of course, broaden the patient population. So we found that to be a rather effective approach, and we've even now started to consider other remote med info support that could be provided as well to make sure that as we penetrate deeper into complex biologics, be they bispecifics or ADCs, that we are able to go shoulder to shoulder with the community and the practicing physicians to support the treatment modality that we're out there with. But Roger, I don't know if you'd add anything.

Roger Dansey ***Pfizer Inc. - Chief Development Officer, Pfizer Oncology***

I can add. So PADCEV has been on the market for a while. In the Seagen era, we spent a significant amount of time educating because this was a new modality, to make sure physicians understood the early side effect profile, how to manage rash, how to manage peripheral neuropathy. So that was where a lot of the focus at Seagen Medical is to make sure that the prescribers actually had the information were properly prepared.

And KEYTRUDA has been around for a while. So it's not like that profile is particularly a mystery to anyone. And the 2 drugs together

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don't amplify. There's not like you've suddenly got a whole new safety profile you have to deal with. So you've got 2 approved agents, both in the hands of the physicians who are going to prescribe them together as opposed to a part. And so there's no surprise to me because PADCEV was used widely -- is used widely in the community as a monotherapy that it would continue to be adopted as a combination. I think you heard very eloquently from Tom earlier around just what's it like to use these drugs in the real world outside of a clinical trial.

Chris Boshoff ***Pfizer Inc. - Executive VP & Chief Oncology Officer***

And then I'll start with the question regarding placement of disitamab, and then I think Roger can add to that as well. So I look at bladder cancer now where lung cancer was 2 decades ago, very homogeneous population being treated essentially up till now for the last 4 decades with platinum-based chemotherapy. So for bladder cancer, we're not splicing up the pie. The pie will get bigger now, with more optionality for patients, more optionality for physicians potentially sequencing in the future. And then optionality also in terms of side effects, that's different between these 2 compounds. So we're very encouraged to develop disitamab as quick as possible for that up to 50% of patients with HER2/1-positive and higher. Roger?

Roger Dansey ***Pfizer Inc. - Chief Development Officer, Pfizer Oncology***

Yes. And I think Tom made a good -- so we don't have the full profile of disitamab, and we were encouraged by the early data. When we understand its full efficacy and safety profile, we'll be able to make judgments around the 2 molecules, where the benefit may be, where it may not be.

I think Tom made this point earlier, which is -- and you can see how the PADCEV program is moving earlier in a substantial way. And the treatment paradigm in muscle-invasive bladder cancer, for example, is fixed. It's not like it's an open-ended therapy. You give 3 cycles of this and then 6 cycles of that and you're done. One could easily imagine if PADCEV moves into that circumstance. And then in a later line, you could come back with, say, an alternative target potentially was the same payload. So there's lots of opportunity for DV in urothelial cancer.

David Reed Risinger ***Leerink Partners LLC, Research Division - Senior MD & Senior Research Analyst***

Dave Risinger from Leerink Partners. I have 2 questions on the CDK4 and on ELREXFIO. So on the CDK4, could you provide a little bit more color on the head-to-head trial plans and potential timing for readout versus CDK4/6? And then with respect to ELREXFIO, with respect to the profile, could you just compare and contrast it with linvoseltamab, which will be coming to market in the next few years?

Chris Boshoff ***Pfizer Inc. - Executive VP & Chief Oncology Officer***

Okay. So just on the first one, just for clarity, are you referring to the CDK4 first -- planned future first line study or the second line study, which is currently -- which has now started?

David Reed Risinger ***Leerink Partners LLC, Research Division - Senior MD & Senior Research Analyst***

The planned future first line.

Chris Boshoff ***Pfizer Inc. - Executive VP & Chief Oncology Officer***

Yes. The planned future, we're still planning the trial. But anything to add on that, Roger?

Roger Dansey ***Pfizer Inc. - Chief Development Officer, Pfizer Oncology***

I think we disclosed time lines, which was, I think, the second half of this year.

Suneet Varma ***Pfizer Inc. - Commercial President, Pfizer Oncology***

This year, yes. So there will be CDK4 plus AI studies by the end of this year.

Chris Boshoff ***Pfizer Inc. - Executive VP & Chief Oncology Officer***

So we'll provide more color closer to time...

Roger Dansey ***Pfizer Inc. - Chief Development Officer, Pfizer Oncology***

Yes. When we have the plan more baked, we will share.

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David Reed Risinger ***Leerink Partners LLC, Research Division - Senior MD & Senior Research Analyst***

Okay. Yes, I was just curious...

Chris Boshoff ***Pfizer Inc. - Executive VP & Chief Oncology Officer***

For instance, is it one specific CDK4 as a comparator or physician's choice CDK4/6, that -- yes, we're working through that. Good question, though.

And then the next one, I was going to ask Akos to comment on the ELREXFIO question.

Akos Czibere ***Pfizer Inc. - Therapeutic Area Development Head for Hematology-Oncology, Pfizer Oncology***

I appreciate the question. I do think we're very encouraged with the data that we're seeing coming out of the MagnetisMM-3 study, right, at exceptional durability, the high CRA, the durability of response in those patients with CR, long median PFS, 17 months, subcutaneous formulation, flexible dosing. So we do think that, that sets ELREXFIO up to be potentially the bispecific of choice, and we'll just have to see how data from other competitors evolves over time. But we do think that with the timing of market entry, just the overall profile, we're well positioned with ELREXFIO.

Chris Boshoff ***Pfizer Inc. - Executive VP & Chief Oncology Officer***

And the wall of clinical trials, we're now building with ELREXFIO.

Susan Chor ***BofA Securities - Equity Research Associate***

Susan from Bank of America. So I have 2 questions. One on ADC technology and one commercial. We've seen that different cytotoxic payloads work with the same targets, Trop-2 and HER2 come to mind. Have you guys looked at different combinations of cytotoxic payloads with different targets? And what's the strategy or biologic rationale for why certain targets work better with certain payloads? And then I'll ask a commercial after...

Chris Boshoff ***Pfizer Inc. - Executive VP & Chief Oncology Officer***

We'll start with that one, and I'll ask Scott because this -- he's developed and discovered so many of these. Scott?

Scott Peterson ***Pfizer Inc. - Head of ADC Discovery and Cancer Immunology, Pfizer Oncology***

Yes. It's a great question. I think in some cases, the tolerability profile really becomes the dominant driver. For example, with Trop-2, I think we found that like an MMAE payload is not well tolerated. But interestingly, topoisomerase I drug linker is pretty well-tolerated and active.

I think there's also a lot of work that goes into thinking about the disease profile and what mechanisms of action might be best suited for those diseases. We've spent time looking at gene expression profiles and how they correlate with susceptibility to different classes of payloads preclinically and then ask the question, could those be predictive clinically to help guide our directionality for pairing drug linkers, payloads and different antibodies to go into different diseases.

Chris Boshoff ***Pfizer Inc. - Executive VP & Chief Oncology Officer***

I think it was a question on combination payload. Was combination payload approach or combination ADCs, was the question?

Susan Chor ***BofA Securities - Equity Research Associate***

I think he answered it, but just if you guys have looked at different payloads with different target. It sounds like yes.

Chris Boshoff ***Pfizer Inc. - Executive VP & Chief Oncology Officer***

I mean the present -- oncology is a combination environment. And suddenly MOAs are basically the sort of standard approach. So I mean, hypothetically, you can construct a single ADC with double payloads or you could have 2 ADCs, same target, 2 different payloads. There are lots of ways of potentially slicing that, and I'm personally interested in exploring that down the road, but we're still defining the baseline in terms of payload activity and disease.

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Susan Chor ***BofA Securities - Equity Research Associate***

So just on the commercial, I think I heard that you guys have 100% integrated Seagen and Pfizer's commercial units. How -- were there commercial metrics that you guys are tracking to sort of decide that we're done, this integration is complete. Just how do we think about that?

Chris Boshoff ***Pfizer Inc. - Executive VP & Chief Oncology Officer***

So the culture for integration continues. That's very important, to continue the culture and continue the meetings and continue the interactions. So that is not just complete. But integration terms and establishing teams, who are the teams? What is the structure, that has been done. Do you want to add to that?

Suneet Varma ***Pfizer Inc. - Commercial President, Pfizer Oncology***

Yes, absolutely. I think that it would be unfair to say that there's not more work to be done. There's always work to be done in any organization, integrated or not, because we're constantly evolving and adapting to what we think the opportunities are. When we say it's fully operational, I think the key thing to keep in mind is that we did a lot of work, a lot of planning in 2023 pre close, to be ready to hit the ground running as soon as we could, and that's in fact what's happened.

Now there were some activities that we said, okay, this is going to be a post-close activity, because it had to be for a variety of reasons, and those activities will still go on. But whether you want to say we're 80-20 or 90-10, the vast majority of the integration activities are done and now our new leaders in place and they're going to adapt as they normally would and operate as they normally would.

I would say just one thing that I'm always -- we've seen in practice as you look at what's the performance and the disruption to get to your point about metrics post close. Do you see a dip in revenues or calls? Do you see disruptions in terms of retention or colleagues? We're looking at all of those. And I'm pleased to say that now we're 75 days in, we are at or above the metrics that we established. So early signs are good. More to be written, but absolutely off to a start in measurements in that domain.

Chris Boshoff ***Pfizer Inc. - Executive VP & Chief Oncology Officer***

Last question, and then we'll wrap up.

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

Evan Seigerman from BMO. So I just have one question to final -- kind of wrap everything up. Clearly, Seagen in oncology is the most important growth driver for Pfizer between now and the end of the decade. You put up a slide that said driving growth through potential near-term launches, what are the 2 or 3 assets or indications on that slide that you think will be -- contribute most to the growth profile between now and 2030?

Chris Boshoff ***Pfizer Inc. - Executive VP & Chief Oncology Officer***

Do you want to...

Suneet Varma ***Pfizer Inc. - Commercial President, Pfizer Oncology***

Go ahead, Chris.

Chris Boshoff ***Pfizer Inc. - Executive VP & Chief Oncology Officer***

So we haven't given for individual medicines. We haven't...

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

What are you most excited about?

Chris Boshoff ***Pfizer Inc. - Executive VP & Chief Oncology Officer***

Exactly. And then we indicated and we are excited that we believe there could be 8-plus blockbusters. I think in the near term, we are excited about the data we're now seeing with something like LORBRENA, which is already approved. We're obviously excited about ELREXFIO. We're obviously excited about what's happening now with PADCEV and what can be achieved with PADCEV. Atirmociclib, for

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us, is a very important new medicine. And what we're doing with prostate cancer with the EZH2 inhibitor, if we can get that going and get those Phase 3 studies start this year, that could be success as well.

And of course, in the near term, there's one in prostate cancer, TALZENNA. If we get that 30% of the population get patients tested both for the current indication, castration-resistant, and then tested for the new indication we're expecting next year if the study is successful and the castration sensitive, that could be another very significant opportunity. I think 2 of the earlier things we've seen today that I hope stimulated interest is around sigvotatug vedotin, the integrin beta-6, as well as I think it was a surprise for many, the PD-L1 ADC that, that really looks like something that could be developed beyond just head and neck cancers. Are there others you would like to point?

Suneet Varma ***Pfizer Inc. - Commercial President, Pfizer Oncology***

It's a good question.

Chris Boshoff ***Pfizer Inc. - Executive VP & Chief Oncology Officer***

I listed actually 10 for you.

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

It's 2 or 3, but it's all good. Thanks, Chris.

Chris Boshoff ***Pfizer Inc. - Executive VP & Chief Oncology Officer***

Okay. Thank you. Thank you. So thank you very much. Thanks for the panel. We're going to complete now. Thanks for all the questions. We hope we've given you a clear picture of our strategy and our science and opportunity for the future. We have many potential significant catalysts, as we just discussed, anticipated through the first half of 2025 spanning our entire portfolio.

First is a continued focus on our priority indication launches this year for PADCEV, XTANDI, from the EMBARK study -- TALZENNA and XTANDI and ELREXFIO. We also anticipate 7 major Phase 3 readouts and several study starts across all of our main tumor types. And as you can see, year 3 of these Phase 3 programs have just started, already enrolling. Two is not listed yet, it's also enrolling, disitamab, the 2 disitamab studies. One second line, potentially registrational and disitamab plus pembrolizumab in first line.

In fact, we have recently initiated these 3 studies. Just to list them again: atirmociclib in metastatic breast cancer; sigvotatug vedotin in non-small cell lung cancer; and the additional trial for ELREXFIO in the post-CD38 multiple myeloma setting.

Lastly, we have a very productive early pipeline, with 8 or more new molecular entities with first in-patient study starts anticipated. We also have key data readouts, as I've just mentioned, which will be PD-L1, ADC and the B7H4 ADC. And as you've heard earlier today, we expect to make decisions on whether to accelerate these 2 programs into registration strategies will be done in the next 6 to 12 months.

Looking further out, we have a broad clinical development pipeline that we believe has the potential to drive long-term sustainable growth through 2030. Starting in the second half of 2025, looking at the currently ongoing or planned Phase 3 programs, these are not new programs. These are current programs already being planned, all being recruited. We have a continuous stream of opportunities, including 17 potential readouts.

To summarize, the power of our combined expertise, broad portfolio and global scale will allow us to strengthen our core business, drive long-term sustainable growth and propel the next wave of oncology innovation. Pfizer Oncology is up and running, and we are accelerating breakthroughs that would change patients' lives.

Thank you very much. I'm now going to ask Albert to come up for a few additional comments. Thank you.

Albert Bourla ***Pfizer Inc. - Chairman of the Board & CEO***

Thank you, Chris, and I was about to say, please, let's give a round of applause for the team that I feel very proud of, so let's do it.

So it has been a very special afternoon for all of us, I hope, and for me, of course. And we could not have made it happen without all of

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you joining us here today and online. We -- I was getting constantly the number of people that were online and was growing into numbers that I have never seen before. So apparently, the oncology attracts a lot of attention, and Pfizer attracts a lot of attention in the beginning of this year. We have been tremendous -- at the end, you have been tremendous on this, to sit it for us for 4 hours. And I hope you agree that it was worth it.

When we first announced the proposed acquisition of Seagen, it was nearly a year ago. I talked about Seagen's ADC platform and how important I felt it is and about its growing in-line medicines and novel pipeline and how we count it all, and about its greatest assets, which are the people of Seagen.

Now I have the privilege this afternoon of hearing about me, together with you, I purposely didn't see a rehearsal of the whole thing because I wanted to have the same experience like the audience on that. And of course, because I trust this team more than anything else. So together with you, I had the privilege to hear about Pfizer's ADC platform and Pfizer's potential for growth and innovation through this pipeline and of course, Pfizer's people.

And however, Pfizer Oncology is not just a collection of strengths from Pfizer and Seagen, as I hope you have seen, the new Pfizer Oncology is a true end-to-end organization that unite the best from Pfizer and Seagen to become something greater than what the 2 companies were before.

With our combined expertise, broad portfolio and global scale, we believe we can do something totally special, accelerate breakthroughs to help people with cancer live better and longer lives. So this is why when you heard me share Pfizer's 5 strategic priorities when you interviewed me in JPMorgan, the first one that we started was achieve world-class oncology leadership, and that's what we are working tirelessly to execute right now.

And I think you have seen today that we are on a good path towards achieving something like that. We have an impactful strategy which is grounded in key focus areas, and we believe we can make a difference. We have a deep and diverse portfolio, as you could see, assets with blockbuster potential and multiple near- and midterm catalysts to drive innovation and longer-term sustainable growth.

Our goal, as you heard, is to double the number of patients treated with our cancer medicines by year 2030. And we're operating from a position of strength to make this happen. Of course, I want to remind everyone that Pfizer is not only oncology, and that we have other 4 priorities that I have spoken about them in the beginning of the year, which are just as important for Pfizer. And I want to take a moment to remind everyone.

First, it is to maximize the performance of our new products, both newly launched and acquired, with a relentless focus on execution, driven by our commercial leaders in the U.S., international, and of course, oncology. You have seen, Suneet, very important. We never have -- you never have a second chance to make the first impression. We launched this product. I think we have now provided some fixes in our commercial machine and we hope that this will deliver results that we all expect. Second priority, delivering the next wave of pipeline innovation outside of oncology and new vaccine, with focus on vaccines and the effective metabolic diseases and inflammatory diseases. Third, expand our margins. And we start with realigning our cost base, driven by our goal to achieve $4 billion in annual net cost savings by the end of this year. We feel very confident, but we will do that. And of course, fourth, use the capital in a way that will enhance shareholder value, including our commitment to a growing dividend. But it is a fundamental part of our investment thesis right now.

As I mentioned in January, we plan to provide updates throughout the year on how we are advancing those strategic priorities. And of course, we will see the results of the first quarter in -- I guess, in April. You can consider today as an update on priority #1: How we plan to achieve leadership in oncology. Thank you again. Thank you, Chris. Thank you to your team. Thank you, Dr. Tom Powles. Thank you very much for coming here. Francesca, and the IR team, and thank you all very much for spending your afternoon with us. Now for those that -- you, who are here, we have an incentive with some wine and hors d'oeuvres. And please join us in the reception that follows. Thank you very much, everyone.

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