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PFE.N - Pfizer Pflash: A Spotlight on Pfizer Breast Cancer Portfolio

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OVERVIEW:

Company Summary

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PRESENTATION

Operator

Good day everyone, and welcome to Pfizer Pflash, a spotlight on Pfizer's breast cancer portfolio. Today's call is being recorded.

At this time, I would like to turn the call over to Francesca DeMartino, Chief Investor relations Officer and Senior Vice President. Please go ahead, ma'am.

Francesca DeMartino - *Pfizer Inc - Chief Investor Relations Officer*

Thank you and good morning everyone. I'm Francesca DeMartino, Chief Investor Relations Officer. On behalf of the Pfizer team, thank you for joining us for our fifth Pfizer Pflash webcast. Today's call will be recorded and will be available for replay on our IR website at pfizer.com.

As a reminder, our Pfizer Pflash series is intended to serve as an educational deep dive into our pipeline products and people. Each call will spotlight a specific product, therapeutic area, or growth initiative, and give you an opportunity to hear from and interact with our business leaders.

Today's session will begin with a short conversation followed by live Q&A. As a reminder, this call is intended only for the investment community, including our sell-side analysts and institutional investors. If you're unable to join the entirety of the event, you can find the replay available on our IR website.

I want to note that on today's call, we will be making forward-looking statements. I encourage you to view slide 2 in our presentation and the disclosures in our SEC filings, which are all available on our IR website at pfizer.com. Forward-looking statements on the call are subject to substantial risks and uncertainties speak only as of the call's original date, and we undertake no obligation to update or revise any of the statements. With that, let's get started.

As breast cancer is a key therapeutic area of focus for Pfizer, with a portfolio that seeks to address multiple breast cancer subtypes in patient populations. Today, we will provide insight into our breast cancer strategy and pipeline that we believe has the potential to be a key driver of growth for our oncology business. It is a privilege to have you all with us as we discuss Pfizer's breast cancer portfolio.

Before we move to the main discussion, let me take a moment to introduce our speakers, Megan O'Meara, Head of Oncology, Early Clinical Development; and Johanna Bendell, Chief Development Officer for Oncology. Megan and Johanna each have central roles in the clinical development of Pfizer's innovative oncology medicines and product candidates. Megan and Johanna, welcome and thank you so much for joining us today.

Can you please start by introducing yourselves and give a brief overview of your current role and experience?

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

Thank you, Francesca. I'm happy to be here today with Johanna to talk about Pfizer's progress in developing potential new medicines for the treatment of breast cancer. In my role as Pfizer's Head of Early Clinical Development and Oncology, I'm responsible for clinical development across Pfizer's early stage oncology portfolio, developing the clinical strategy that creates the foundation for our programs to move into pivotal studies.

I joined Pfizer through the acquisition of Seagen, where I spent more than 12 years, and most recently led both early and late stage clinical development.

And with that, I'll turn it over to Johanna.

Johanna Bendell - *Pfizer Inc - Chief Development Officer, Oncology*

Thank you, Megan. I'm Johanna Bendell, Chief Development Officer for Oncology, and I'm responsible for the strategy and execution of clinical development for all of Pfizer's oncology late stage portfolio.

I very recently joined Pfizer from Roche, where I served as Global Head of Oncology, leading discovery and early clinical development.

I'm very excited to be joining Pfizer and looking forward to working with the thousands of Pfizer colleagues who every day strive to deliver new and better medicines to patients with cancer.

And with that, I'll turn it back over to Francesca.

Francesca DeMartino - *Pfizer Inc - Chief Investor Relations Officer*

Thank you both for your introduction, and let's get started. Johanna, I'll ask you to kick things off today. Would you please give us a brief reminder of Pfizer's oncology strategy and where breast cancer fits into the oncology portfolio.

Johanna Bendell - *Pfizer Inc - Chief Development Officer, Oncology*

Thank you, Francesca. I'd be happy to get us started. At a high level, our strategy is driven by our goal of accelerating breakthroughs that can help people with cancer live better and longer lives. Pfizer's oncology strategy can be described in two dimensions.

The first dimension includes three core therapeutic modalities, each of which are enabled by deep technical expertise. First are small molecules where we have established world-class drug discovery and medicinal chemistry expertise. We also have core strengths and large molecular biologics enabled by our capabilities in protein engineering and antibody design.

And finally, with the acquisition of Seagen, we have an industry-leading platform and know-how to deliver ADCs or antibody drug conjugates, a modality that very neatly sits at the intersection of small molecules and biologics.

Here we are focused on the next generation of potentially better and safer ADCs, leveraging new targets with improved conjugation technologies and highly differentiated anti-cancer payloads.

The second dimension covers the cancer indications that we are prioritizing. Specifically, we continue to build on Pfizer's established presence in breast cancer, as we will focus on today, along with Genitourinary cancers, Hematologic Malignancies, and Thoracic cancers. We also remained interested in capitalizing on emerging opportunities in Gastrointestinal cancers.

For example, the practice changing results with the combination of BRAFTOVI, cetuximab, and modified FOLFOX6, as reported recently at ASCO for our breakwater trial in BRAF-mutant colorectal cancer.

Francesca DeMartino - *Pfizer Inc - Chief Investor Relations Officer*

Thanks, Johanna. To help orient the discussion, can you please provide a brief overview of breast cancer and the ways in which physicians classify and treat breast cancer?

Johanna Bendell - *Pfizer Inc - Chief Development Officer, Oncology*

Certainly. Following many years of research, we know that breast cancer is a collection of multiple diseases and that the details for each patient are essential to the treatment strategy. As shown in the left panel, one straightforward way to classify breast cancer is as early, locally advanced, or metastatic, with worsening prognosis as one moves from early to metastatic disease.

These classifications differ based on the types of cells involved and whether the cancerous cells have spread. Early breast cancer is described by disease that has not spread beyond the breast or axillary lymph nodes and is commonly treated with combinations of surgery, including lumpectomy or mastectomy and radiation therapy, followed by hormone therapy.

Locally advanced breast cancer is where cancer cells have spread into the surrounding areas, but not yet to distant locations. And in metastatic disease, the spread of cancer cells is more significant and includes distant sites in the body. Treatment of later stage and or metastatic disease typically involves systemic therapies such as combinations of hormone therapy, chemotherapy, targeted therapy, and immunotherapy.

Another way to classify breast cancer is by the molecular signatures, such as protein expression patterns or specific genetic mutations. For the approximately 330,000 women and men diagnosed with breast cancer in the US each year, this classification is key to guiding systemic therapy decisions.

The molecular signature with the highest incidence is expression of a hormone receptor, often abbreviated as HR, which includes estrogen and progesterone receptors. A second subset is marked by the expression of human epidermal growth factor receptor 2, abbreviated as HER2.

Tumors may be positive or negative for HR and HER2 expression. The majority, approximately 65% to 70% of breast cancers are HR+, HER2 negative. Treatment of HR+ breast cancer includes hormone therapy, chemotherapy, and targeted therapy. HER2 positive cancers occur in about 15% to 20% of patients, and treatment includes HER2 targeted ADCs and Tyrosine kinase inhibitors.

Triple negative breast cancer or TNBC is a subtype characterized by a lack of expression of estrogen receptor, progesterone receptor, and HER2, and represents approximately 10% to 15% of patients. The absence of treatment currently relies largely on general cytotoxic, oh sorry, -- the absence of these HER2 and HR targets means that targeted therapies are less relevant for TNBC.

Instead, treatment currently relies largely on General Cytotoxic agents such as Taxanes and platinum-based chemotherapy. There's also a subgroup of patients with low expression of HER2, referred to as HER2 low patients, that nests across the HR posit and TNBC groups.

Francesca DeMartino - *Pfizer Inc - Chief Investor Relations Officer*

Thank you. That's a very helpful anchor for the discussion. Let's talk briefly about IBRANCE, a medicine that has been a cornerstone in building Pfizer's breast cancer franchise. How is Pfizer thinking about the future of IBRANCE and its broader breast cancer franchise with IBRANCE coming off patent in the next few years?

Johanna Bendell - *Pfizer Inc - Chief Development Officer, Oncology*

IBRANCE is Pfizer's CDK4/6 Inhibitor selective tyrosine kinase inhibitors that has become a cell cycle inhibitor backbone therapy for breast cancer treatment. Since its initial FDA approval 10 years ago, IBRANCE has continued to demonstrate its value as a standard of care first line treatment for HR+ HER2 negative metastatic breast cancer, and has now been prescribed to over 838,000 patients and approved in 108 countries.

And IBRANCE is still delivering important results for patients, including the recent FDA approval of the addition of inavolisib, a PI3 kinase inhibitor to IBRANCE plus fulvestrant, which was shown in the INAVO120 study to improve overall survival in PI3 PIK3CA mutated, HR+, HER2 negative, endocrine resistant, locally advanced, and metastatic breast cancer.

This cross labeling also provides an additional measure of differentiation versus other CDK46 inhibitors. In addition, the readout for the PATINA study, in which IBRANCE was added to standard of care first line maintenance, demonstrated improved progression free survival in HR+, HER2 positive metastatic breast cancer.

Results of the PATINA study were presented at the San Antonio Breast Cancer Conference last December and may provide another future opportunity for label expansion.

In short, IBRANCE has established a strong legacy in breast cancer treatment, and we are expanding on this legacy by delivering important breast cancer medicines for patients and building a rich pipeline of potential therapies across the breast cancer spectrum.

Francesca DeMartino - *Pfizer Inc - Chief Investor Relations Officer*

Thank you, Johanna. At this point, I'd like to turn the discussion to the pipeline. Can you walk us through Pfizer's breast cancer pipeline and some of the key opportunities for growth?

Johanna Bendell - *Pfizer Inc - Chief Development Officer, Oncology*

Absolutely. Our clinical pipeline for breast cancer includes small molecules and ADCs and spans from the early and neoadjuvant settings, all the way to later lines of therapy for patients whose disease has relapsed or progressed following prior therapies.

We see multiple avenues to potentially address unmet need and drive growth. First, our potential label expansion opportunities for approved products, such as moving to Kaiser or HER2 inhibitor into earlier lines of therapy, including first line maintenance and adjuvant settings for HER2 positive disease.

Another opportunity is for IBRANCE in HR+ HER2 positive maintenance, as well as frontline therapy and endocrine resistant HR+, HER2 negative, PIK3CA mutant settings.

A second path to potential growth is the development plan for our highly selective CDK4 Inhibitor, Atirmociclib. Our objectives here are to position Atirmo as the potential next generation cell cycle therapy backbone, highlight its potential in both adjuvant and frontline settings across HER2 negative and potentially HER2 positive disease, and identify potential advantages over competitor CDK4/6 inhibitors such as Ribociclib and Abemaciclib.

A third path to potential growth is with our pipeline of multiple novel agents and mechanisms of action, including our KAT6 inhibitor, our CDK-2 inhibitor, and the HER2 targeted ADC Disitamab Vedotin or DV. These programs seek to test the potential for deeper and more durable responses, the potential to address mechanisms of resistance, and the potential for impact in TNBC.

Drawing on our leading discovery and development capabilities across small molecules, ADCs, and non-ADC biologics. We also have discovery and preclinical stage programs that we look forward to sharing in the future.

Francesca DeMartino - *Pfizer Inc - Chief Investor Relations Officer*

Let's take a deeper dive on a Atirmociclib. Megan, what makes a selective CDK4 inhibitor so interesting? What are the plans for the program and how are they supported by the data you have seen so far?

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

Atirmociclib is our highly selective CDK4 inhibitor that was discovered and developed in-house. Our objectives in developing a next-gen CDK4 inhibitor for breast cancer were twofold. First, we wanted to maximize CDK4 inhibition in order to maximize efficacy. The majority of HR+ breast cancers express low levels of CDK6, making CDK4 the likely cell cycle driver in this subtype. In addition, complete CDK4 inhibition with CDK4/6 inhibitors is quite challenging due to the potential for dose limiting hematologic adverse events.

Which brings us to the second objective, which is to reduce the incidence and severity of these hematologic adverse events. CDK4/6 inhibitors can lead to severe neutropenia, which is a subtype of a low white blood cell count that can lead to potential risk for infections in some patients.

And these adverse events are largely due to the contribution of CDK6 inhibition. Thus, by enhancing the selectivity for CDK4, we believe we can potentially achieve both goals. This strategy led to a Atirmociclib, a potentially best in class inhibitor, with a 33-fold greater selectivity for CDK4 versus CDK6.

Our clinical development plans for Atirmo are focused on the adjuvant and first line settings, and we have been very encouraged by the data, the clinical data we've seen. Last year at San Antonio Breast Cancer Symposium, we reported data for a Atirmo plus Letrozole in the frontline setting for HR+ HER2 negative metastatic breast cancer.

Preliminary efficacy from a Phase 1/2 study is shown in the waterfall plot on the left side. For those not familiar with waterfall plots, what you want to see is the bars going down, as you can see on the left-hand side of this slide, and those bars going down are associated with tumor shrinkage.

And specifically, the objective response rate, or ORR was very promising at 61%, and numerically higher than approved CDK4/6 inhibitors in similar treatment settings. While the median duration of response was not reached, we were encouraged to see that the responses appeared durable and tended to deepen with increasing duration of treatment.

Similarly, the clinical benefit rate, or CBR, which is the aggregate frequency of complete response, partial response, and stable disease, was 94%. The median progression free survival, or PFS, was not yet reached at 16.5 months median duration of follow-up, and 25 of 34 patients, or 74%, were continuing treatment without disease progression at the data cut-off.

In addition, the ORR and CBR were largely independent of driver mutations such as PIK3CA, AKT1, and PTEN. Importantly, the data also highlight a potentially differentiated safety and tolerability profile relative to approved CDK4/6 inhibitors, particularly with respect to neutropenia and gastrointestinal side effects such as diarrhea.

Importantly, there were no grade four or five treatment-related adverse events. An improved adverse event profile may in turn lead to potentially fewer dose reductions and discontinuations for a Atirmo. Which at 9% and 3% respectively are meaningfully lower than CDK4/6 inhibitors such as ribociclib, abemaciclib, and palbociclib.

Ultimately, this can potentially allow for continuous dosing schedules, a longer duration of therapy, and improved clinical benefit. These and other data have given us confidence to move forward with our four light three study, a pivotal trial testing a Atirmo versus investigator's choice of CDK4/6 inhibitor, each in combination with Letrozole, as frontline treatment in HR+, HER2 negative, locally advanced, and metastatic breast cancer.

The study, which is actively enrolling, has a progression free survival primary endpoint and secondary endpoints that include overall survival and duration of response.

In early breast cancer, we have FourLight-2, our controlled Phase 2 trial in the neoadjuvant setting, testing a Atirmo plus Letrozole versus Letrozole alone. The study is evaluating treatment over a period of 14 days and looking at expression of Ki-67, a potentially prognostic marker for HR+ early breast cancer. This study is also ongoing, and we anticipate data in the fourth quarter of this year.

Francesca DeMartino - *Pfizer Inc - Chief Investor Relations Officer*

Thanks, Megan. You mentioned focusing on the front line and adjuvant settings with the Atirmo, and earlier we saw in the pipeline that the KAT6 inhibitor is focused on later lines of therapy. Can you expand on the rationale for that decision, as well as the overall status of the KAT6 program?

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

Absolutely. Our KAT6 inhibitor, also discovered in-house, is a potential first in class, potent and selective inhibitor of the epigenetic modifiers KAT6A/B. The figure on the left side shows the role of KAT6 in transcriptional control via its Lysine acetyltransferase activity, and how inhibition of KAT6 reduces histone acetylation and in turn decreases gene activation.

Interestingly, KAT6 is a known regulator of estrogen receptor alpha expression, itself the product of the ESR1 gene and one of the markers of HR+ breast cancer. Estrogen receptor alpha is amplified in about 12% of HR+ breast cancer, and elevated expression is associated with poor patient survival outcomes.

On the right side of the slide are Immunohistochemistry data from a mouse tumor model showing the high levels of estrogen receptor expression indicated by the brown color. When these mice receive the KAT6 inhibitor, the levels of estrogen receptor are greatly diminished, demonstrating pharmacologic activity of KAT6 inhibition on levels of estrogen receptor.

A very interesting part of the story is the potential for KAT6 inhibition to overcome resistance to endocrine and CDK4/6 therapy. For example, mutations in the ESR1 gene can drive resistance to endocrine therapy.

In a frontline setting, approximately 5% of patients have an ESR1 mutation. However, in second line settings, this number jumps to approximately 40%. All of this provides a compelling rationale to develop our KAT6 inhibitor for second line and later line settings.

Just like atirmociclib, data from our KAT6 inhibitor clinical studies have been very encouraging. We presented exciting Phase 1 data at San Antonio Breast Cancer Symposium in 2024 and just recently updated those data at ASCO.

Results were presented for second line treatment for ER positive, HER2 negative metastatic breast cancer patients who had prior treatment with a CDK4/6 inhibitor.

As reflected in the spider plot and data on the left side, KAT6 inhibitor plus fulvestrant provided both deep and durable responses in the Phase 1 study. As you can see on the left, that's the spider plot. What you want to see is the bars going down and continuing down for durability of response.

In a cohort of 43 patients and with a median follow-up of 21.9 months, results included a 37.2% objective response rate, median progression free survival of 10.7 months, and a median duration of response of 15.8 months.

Anti-tumor activity was observed regardless of the presence or absence of actionable mutations, endocrine sensitivity, duration of prior CDK4/6 inhibitor treatment. Prior fulvestrant treatment, and second line or later therapy.

Also, as presented at ASCO, we have identified a dose for a Phase 3 development that delivered on key metrics, including tolerability, pharmacokinetics, pharmacodynamics, and encouraging anti-tumor activity. We anticipate starting a pivotal study for our KAT6 inhibitor in combination with fulvestrant in the second half of 2025.

Francesca DeMartino - *Pfizer Inc - Chief Investor Relations Officer*

Thank you, Megan. Definitely a lot to look forward to for both Atirmo and KAT6. Sticking with the novel MOA category, can you briefly speak to the status and scientific rationale behind the CDK2 inhibitor program?

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

Yes. Our CDK2 inhibitor is a potentially first in class molecule that is designed to delay or overcome resistance to CDK4/6 inhibitors. As shown on the left panel, CDK2 and Cyclin E are key to cell cycle progression. Their absence can sensitize cancer cells to CDK4/6 inhibition, potentially providing a path to deeper and more durable responses with CDK4 inhibitors.

CDK2 has also been implicated in mechanisms of resistance to the CDK4/6 inhibitor palbociclib. And in pre-clinical testing, we've seen that the combination of a Atirmociclib and our CDK2 inhibitor has synergistic anti-tumor activity in palbo-sensitive and resistant positive metastatic breast cancer models.

In the middle panel are data from our genome-wide CRISPR screen. The data support CDK2 as both a driver of resistance to CDK4/6 inhibition, but also a sensitizer to CDK4/6 inhibitors, in this case reflected by a lower beta score.

Finally, shown on the right panel, gene expression analyses from the Phase 3 PALOMA trial evaluating IBRANCE plus fulvestrant, show a reduction in median PFS when accompanied by high Cyclin E expression in patients receiving IBRANCE plus fulvestrant.

Collectively, these data support a role for Cyclin E and thus CDK2 in resistance to IBRANCE. Early clinical data in heavily pre-treated patients, as reported at ESMO 2024, showed promising early anti tumor activity for the combination of a Atirmo plus CDK2 inhibitor and HR+ HER2 negative metastatic breast cancer.

In this data set, all 18 patients had received prior CDK4/6 inhibitors, and the median lines of prior therapy was three, but some patients had seen as many as 14. The results in patients with measurable disease showed an objective response rate of approximately 28%, disease control rate of nearly 56%, and median progression free survival of 8.3 months.

The encouraging data from these later line settings, coupled with data demonstrating CDK2 can not only potentially overcome resistance to CDK4/6 inhibitors, but also mediates sensitization to CDK4/6 inhibition, provided us with confidence to test the Atirmo plus CDK2 combination in frontline settings, and that Phase 1 study is ongoing.

Francesca DeMartino - *Pfizer Inc - Chief Investor Relations Officer*

Megan, thank you so much. Johanna, I'll now come back to you for a couple of late stage programs. Turning first to the Vepdegestrant, what's the status of that program?

Johanna Bendell - *Pfizer Inc - Chief Development Officer, Oncology*

Thanks so much, Francesca. Vepdegestrant or Vepdeg is a molecule of the novel mechanism of action. It's a proteolysis targeting chimera or protag that drives specific degradation of estrogen receptor.

Together with our partner Arvinas, we tested Vepdeg in the Phase 3 VERITAC 2 trial, which compared Vepdeg versus fulvestrant in second line and later ER positive HER2 negative breast cancer.

Data from VERITAC 2 were recently presented at ASCO, and there was also a concurrent publication in the New England Journal of Medicine.

Vepdeg is the first PROTAC degrader to show clinical benefit in a Phase 3 trial with a significantly improved progression-free survival in the ESR1 mutant population. Five months versus 2 months in the Vepdeg arm versus the fulvestrant arm.

The study did not reach statistical significance in the overall population. Overall survival at the key secondary endpoint was not yet mature at the time of analysis. Vepdeg was generally well tolerated, with mostly low grade treatment emergent adverse events, with a safety profile consistent with that observed in previous studies. The data suggests that Vepdeg could potentially play a role in the treatment of ESR1 mutant disease, a group of patients with unmet need.

Arvinas and Pfizer have just recently submitted a new drug application for Vepdeg and is subject to acceptance by the FDA. In addition, we continue to explore opportunities Vepdeg, including in combination with KAT6, where we have added a combination cohort to the ongoing KAT6 inhibitor Phase 1 trial.

Francesca DeMartino - *Pfizer Inc - Chief Investor Relations Officer*

Thanks very much, Johanna. Lastly, I'd like to turn to TUKYSA, Pfizer's small molecule inhibitor of the HER2 receptor tyrosine kinase, that is approved by FDA in second line and later HER2 positive breast cancer and HER2 positive colorectal cancer. We have shared our expectation for another pivotal Phase 3 readout for TUKYSA later this year. Can you remind us of the study if the readout is still on track and what you hope to achieve from it?

Johanna Bendell - *Pfizer Inc - Chief Development Officer, Oncology*

Of course, the Phase 3 study you asked about is HER2CLIMB-05, a pivotal study evaluating the addition of TUKYSA to the frontline maintenance regimen of pertuzumab plus trastuzumab in HER2 positive disease. While TUKYSA is currently approved in the second line and later setting, the goal for HER2CLIMB-05, and the data expected to read out later this year, is to bring TUKYSA into earlier treatment settings, establish a new maintenance backbone, and positively impact more patients.

In addition to HER2CLIMB-05, we also have ongoing Phase 3 trials in the second line and adjuvant settings, with an overarching goal to develop TUKYSA as a backbone tyrosine kinase inhibitor in HER2 positive breast cancer.

Francesca DeMartino - *Pfizer Inc - Chief Investor Relations Officer*

Great. Megan, Johanna, thank you very much for this discussion of Pfizer's breast cancer portfolio. It's clear that there are very active and exciting pipeline in breast cancer that is building on the legacy established with IBRANCE.

As Megan and Johanna have highlighted throughout today's discussion, there are multiple ways in which Pfizer is working to address unmet patient need and drive future growth. Some of the highlights that we have discussed today include the recent label expansion for IBRANCE in combination with inavolisib and fulvestrant. And the PATINA data that may lead to another label expansion opportunity in the maintenance setting.

An upcoming Phase 3 readout for TUKYSA as a maintenance option for HER2 positive breast cancer, a development strategy for a Atirmociclib to potentially be a new cell cycle inhibitor backbone in frontline. And early breast cancer treatment, where the CDK4/6 market alone stood at $12.7 billion in 2024.

A pipeline of molecules with novel mechanism of action, including KAT6, CDK2, and Vepdeg, that have the potential to address mechanisms of resistance as well as potentially provide improved clinical outcomes and additional early stage programs across modalities that we look forward to sharing in the future.

Before we move to Q&A, I'd like to draw your attention to our development path overlaid against US epi data, which should give you a sense of the addressable market for each breast cancer subtype and line of therapy that Pfizer's development programs are seeking to address.

As you can see, there are significant new opportunities, and we believe the collection of assets we've discussed today have the potential to situate Pfizer as a continued leader in the breast cancer space. We're looking forward to sharing updated clinical data, and when relevant, our plans for commercialization.

We will now begin the Q&A session with Megan and Johanna. As a reminder, our Pfizer Pflash series is designed as an educational deep dive into our pipeline programs. I'll therefore kindly ask participants to keep questions focused on breast cancer and the programs discussed today, and to avoid those that would require us to provide forward-looking financial projections. While we're happy to clarify any information shared during the presentation, we will not be offering estimates beyond what has already been communicated. Thanks for your understanding.

With that, we're ready to take the first question, operator, if you could please assemble the queue.

QUESTIONS AND ANSWERS

Operator

(Operator instructions) Chris Schott, JPMorgan.

Chris Schott - *JPMorgan Securities LLC - Analyst*

Great. Thanks so much for the question and doing the call today. I just had two on the CDK4 opportunity, I guess maybe on the first line study. Can you just help us in terms of what you would view as clinically meaningful data in the setting, kind of what's the bar you think you need to show versus the traditional CDK4/6s in order to get broad adoption here?

And then my second question was on the adjuvant setting and sorry if I missed this, but I know you highlighted. The neoadjuvant study you're running, are you also going to look at adjuvant for the product as well, and what would a program look like in in that setting? Thanks so much.

Johanna Bendell - *Pfizer Inc - Chief Development Officer, Oncology*

Thank you so much, Chris, I -- this is Johanna. I'll start and then have Megan chime in. We're very excited about looking at Atirmo in the first line setting because we see this as a potentially new cell cycle inhibitor backbone therapy for patients with first line disease. We know that in for typical CDK4/6 inhibitors, issues include these toxicities that you can see, including neutropenia and diarrhea.

And so we I think clinically meaningful decrease in these toxicities to allow patients to maintain on therapy longer and then potentially have, continued impact on that cell cycle pathway, could improve outcomes, for these patients, both from a toxicity and hopefully prolongation of progression free survival.

So this is what we're aiming for, in first line. And in the adjuvant setting, yes, you heard us mention, we do want to try to bring this forward as well into the adjuvant setting. So we're currently looking at plans for an adjuvant study and they're in discussion right now.

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

Yeah, and just to build on that, I, we're, like we mentioned earlier, we're really encouraged by the data we saw in the Phase 1/2 study with the 61% response rate and 94% clinical benefit rate which you saw the waterfall plot. Almost every tumor was shrinking and we continue to see nice durability. We're able to deliver Atirmo continuously given its tolerability profile and specificity for CDK4. And so we're very encouraged that that Phase 1/2 data set will translate within the pivotal study.

Francesca DeMartino - *Pfizer Inc - Chief Investor Relations Officer*

Operator will take the next question, please.

Operator

Mohit Bansal, Wells Fargo.

Mohit Bansal - *Wells Fargo - Analyst*

Great, thank you very much for taking my question and thanks for this presentation. Just, one question regarding the timelines here, and then your confidence level in the CDK4? So can you help us understand, I mean, you should share some these two data, but what gives you confidence that you would be able to achieve success in the Phase 3 trial based on the small subset of 34 patients here, or is it the biology, is it more expression or more suppression of CDK4 here?

And then the other one is these breast cancer trials take a long time. So how are you thinking about timelines in this context as well as potentially expediting the pathway here, maybe by some kind of enrichment? Thank you.

Johanna Bendell - *Pfizer Inc - Chief Development Officer, Oncology*

Thank you. Maybe I can start with that as we talk about timelines. It's hard for us to comment exactly on timelines just because we continue to see how the trial enrolls. I can comment that the trial is actually accruing at a very good pace. So we're hoping to continue on that pace and get results from this study.

In terms of confidence level, I think we're fairly encouraged even though it's early data and it's a small subset of, it's a small, number of patients that were tested, but I think the responses that we've seen in the Phase 1 study as well as the toxicity differential make us very encouraged.

We know that CDK4 is a major node in the cell cycle pathway, and we hope and think that it's the most responsible node that we can attack to help improve the outcomes for these patients just following the science there. Megan, do you have?

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

Yeah, no, I completely agree, Johanna. I think, we were able to generate a scientific hypothesis around specific targeting at CDK4. We generated a very exciting pre-clinical package that got us excited to bring this to the clinic. And then in the Phase 1/2 study, it was all consistent where we, the scientific hypothesis played out with really strong clinical benefit across this patient population. And so, I think, we're confident in this, in the frontline setting and we're committed to following the Phase 3 through.

Francesca DeMartino - *Pfizer Inc - Chief Investor Relations Officer*

Operator will take the next question.

Operator

Evan Seigerman, BMO Capital Markets.

Malcolm Hoffman - *BMO Capital Markets - Analyst*

Hi, Malcolm on for Evan. Thanks for taking our question. I want to say I appreciate the very comprehensive view of the portfolio today. But -- the team didn't talk much about Disitamab Vedotin. Could you provide a bit of an overview for what the plans are for this asset? Looks like you had noted some opportunities really in the second line plus setting, so, just appreciate any color here. Thanks.

Johanna Bendell - *Pfizer Inc - Chief Development Officer, Oncology*

Yes, thanks so much. So with DV being a HER2, targeting vedotin, we are looking at this in the, in HER2 refractory setting, and we would really like to see, what kind of activity we get for those patients. As we see this data, this will help us understand a bit more where we can think about placing DV in the future. We know that HER2 is a great drug and it's provided a great option for patients with HER2 positive disease, but we also know that there's a lot more opportunity for those patients in terms of further targeting that pathway and bringing more therapies to them.

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

Yeah, and just, this is Megan from a scientific perspective, I think it'll be really interesting to understand, what we learned about sequencing different antibody drug conjugates in this space because there is really remaining unmet medical need post in HER2.

Operator

Vamil Divan, Guggenheim Securities.

Vamil Divan - *Guggenheim Securities LLC - Analyst*

So maybe two. Just on the KAT6 side, so one, appreciate the efficacy you talked about. We do get a lot of questions on the side effect profile there, especially if it's dysgeusia. Can you maybe just talk about that and your views on how manageable that is that you move that product forward and then thought it was interesting you having vepdeg. You mentioned a combo cohort to that Phase 1 trial with the KAT6. So is that a vepdeg fulvestrant combo, or if you can just comment on kind of what you've seen, to add that into the KAT6.

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

Sure. I can take that one to start. So, we're, we continue to be really encouraged about our KAT6 program. This is a potentially, first in class molecule where we've seen, really nice, benefit in activity and heavily pre-treated patients across different, mutational subsets.

And with regard to the safety profile, I think the two most common adverse events that we're seeing include dysgeusia and neutropenia, but these are both manageable. With regard to the dysgeusia, this is a really exclusively low grade dysgeusia we're seeing. And we're watching carefully for

any dose discontinuations and thus far within the Phase 1, we've not seen anybody discontinue treatment due to dysgeusia. It's manageable with dose modifications and dose delays.

With regard to the neutropenia, we've also not seen any negative sequelae related to kind of neutropenia associated infections in these patients. And so, I think we continue to be encouraged by the data.

With regard to the Vepdeg plus KAT6 combination cohort that we just added to the KAT6 Phase 1, this is, that we're not including Vepdeg - fulvestrant, this is Vepdeg plus KAT6 in this space, and we have, we've just started enrolling this cohort, so we don't have any data to report out as of yet.

Operator

Geoff Meacham, Citibank.

Nishant Gandhi - *Citibank - Analyst*

Hey guys, this is Nishant on for Geoff. Thanks for the presentation, really helpful. One of the combinations, you have really printed exciting kind of data in, CDK4 and other combination studies, and, you also have, exciting ADC platform. Just wanted to get your thoughts on, any opportunities there to combine with any other ADCs. I know you have DV, but any opportunities there to combine?

And then second, do you see a potential for KAT6, to combine with any other agents in your pipeline like, atirmociclib or others? Thank you.

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

Sure, I can start and then Johanna, feel free to build upon this. I mean, we're definitely, focused on our, breast as a therapeutic area and we have a really deep pipeline here and this does present us with opportunities for multiple different, internal combinations as well as combinations, with other agents, that are in the clinic.

With CDK4, we really see up with the Atirmo, we see this as the potential to be a future backbone in the frontline HR+, breast cancer space and beyond. And so we're looking to really combine across the spectrum with different breast cancer subsets and mutational subsets within this space, not only with internal combinations, but also with you know PI3 kinase inhibitors and other molecules and this is ongoing.

We also, as mentioned, you have a broad ADC platform and beyond DV we do have other ADCs in the pipeline that have the potential opportunity in the breast cancer space. One example of that is PDL1V or PDL1 Vedotin ADC, which is currently being evaluated in a Phase 1 cohort in PDL1 positive triple negative breast cancer.

So that's another opportunity. We don't have any ongoing combinations with our CDK4 inhibitor and ADCs, but that's something we're looking at as we continue to broaden the life cycle for Atirmo. And then in terms of KAT6 combinations, we've currently prioritized the combination with fulvestrant in the Phase 3 that's about to start later this year. And then we have the ongoing KAT6 plus Vepdeg combination. We are continuing to look at opportunities for KAT6 and other spaces, including other combinations. So more to come on that.

Johanna, anything to add?

Johanna Bendell - *Pfizer Inc - Chief Development Officer, Oncology*

Yeah, I think you said it perfectly, Megan, and I think what we're very excited about at Pfizer is, and I'm really glad that you asked this question. Is the possibility to do these combinations? Like, for instance, with CDK4, prior CDK4/6 inhibitors for their hematologic toxicity profile have limited

us in what we can do in terms of combinations. And so what we think this could open up the door with a more specific CDK4, targeting to be able to actually combine with ADCs and other, molecules that might have a little bit more of an overlapping toxicity profile.

And I think also as Megan alluded to, and it was alluded to in the presentation, there is a pre-clinical pipeline that's coming because we are continuing to follow the science and really continue to follow our focus on the HR+ breast cancer space. So stay tuned.

Operator

Kerry Holford, Berenberg.

Kerry Holford - *Berenberg - Analyst*

Thank you for taking the questions. Two, please. Firstly on the KAT6, would just be interested to hear how you're thinking about the development of this novel drug in the second line setting, given the potential change to first line treatment with your thirds and with your PROTAC emerging. So given that profile change to second line patients, how do you allow for that when you're thinking about KAT6 in the second line.

And then my second question specifically on Vepdeg, the VERITAC-2 study we noted that the US cohorts saw a hazard ratio above 1. So the question is how confident are you that you've got sufficient data to get the approval in the US, we have seen competitors in other cancer types see a delay due to a smaller US cohort with a hazard ratio above one. So just interested to hear your thoughts on that. Is it a risk or not in your view?

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

Maybe I can start on KAT6 and then I'll turn it over to Johanna -- Vepdeg. So, yeah, I think we're, as we continue to follow the science and, place our portfolio of breast cancer molecules and spaces. Where it makes the most sense scientifically, we really see an opportunity in the second line and beyond setting for KAT6 where, we've generated data both pre-clinically and clinically that, this inhibition of KAT6 has the potential to overcome resistance to endocrine therapy, and CDK4/6 therapy.

For example, mutations in ESR1 gene can drive resistance to endocrine therapy. As I mentioned earlier, in the frontline setting, 5% of patients have ESR1, but it jumps to 40% in the second line and beyond. So, again, following the science and this hypothesis, I think we're, we see a really, a rational place for KAT6 in the second line and beyond setting.

And, as mentioned, we're also, we're really encouraged to look at the opportunity with Vepdeg, where, Vepdeg has a particular benefit in the ESR1 mutant population. One scientific question is whether this could unlock opportunity in combination with KAT6 beyond ESR1 mutant disease. And so we're continuing to follow that enroll that cohort and follow that out.

And then I'll turn it over to you for Johanna.

Johanna Bendell - *Pfizer Inc - Chief Development Officer, Oncology*

Yeah. And so, I also wanted to say, Megan, I love what you said. I mean, we are super excited about KAT6, not only in combination with Vepdeg, but just because it can treat patients with endocrine resistance, to be able to use it in a much broader population in the second line. And we really excited to see the potential there.

In terms of the VERITAC-2 study, certainly as we look at subset analysis and small cohorts, I just wanted to call out in the US this definitely was a smaller cohort of patients, so the tightening of the confidence intervals, may be a little bit more difficult, in terms of the smaller numbers, but we're still very confident in the data that was shown for that US patient population in terms of trending towards improvement and progression free survival.

Operator

Terrence Flynn, Morgan Stanley.

Hailey Horowitz - *Morgan Stanley - Analyst*

Hi, this is Hailey on for Terrence. Thanks for taking the question and appreciate the detail on the design of the pivotal Atirmo frontline trial. Can you provide any more information on powering for that trial? Thank you.

Johanna Bendell - *Pfizer Inc - Chief Development Officer, Oncology*

I think right now we haven't disclosed a lot of the study details in terms of the pairing and the statistical plan. We most definitely as we start to present more in the future and have some data to present in the future, we can give you more details about that at that time. That's right.

Francesca DeMartino - *Pfizer Inc - Chief Investor Relations Officer*

Okay, I think that, Operator, if there's no more questions, I'll just move to the close. I want to thank everybody for joining us today for this fifth Pfizer Pflash. Our intention is to continue to do these, particularly on the oncology pipeline as we move through the TAs.

And I know summer's about to start. I want to wish everyone a wonderful summer. We're not yet sure if we'll host one in the coming months or wait until after earnings. And if we don't, we'll catch you at earnings and have, enjoy all the weather that's hopefully turning, at least for those of us in New York. Have a great day. Everybody can disconnect.

Operator

This does conclude today's program. Thank you for your participation. You may disconnect at any time.