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PFE - Pfizer Inc Corporate Call - Oncology Business Review and ASCO Data Presentations

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OVERVIEW:

Co. provided a review of its oncology business and ASCO data.

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PRESENTATION

Operator

Good day, everyone, and welcome to Pfizer's Analyst and Investor Call to Review Oncology Business and ASCO Data Presentations. Today's call is being recorded.

At this time, I would like to turn the call over to Mr. Chuck Triano, Senior Vice President of Investor Relations. Please go ahead, sir.

Chuck Triano - *Pfizer Inc. - SVP of IR*

Thank you, operator. Good afternoon, everyone, and thank you for joining us today to review Pfizer's Oncology business and our presence at ASCO this year.

I'm joined here today by Albert Bourla, Group President of Vaccines, Oncology and Consumer Healthcare; Liz Barrett, President of Pfizer Oncology; and Mace Rothenberg, Head of Clinical Development and Medical Affairs, and Chief Medical Officer for Pfizer Oncology. The slides that will be presented on the call can be viewed on our home page, Pfizer.com, by clicking on the link under the For Investors section, which is located in the lower right-hand corner of the page.

Before we start, I'd like to remind you that our discussions during the call will include forward-looking statements, and that actual results could differ materially from those projected in the forward-looking statements. The factors that could cause actual results to differ are discussed in Pfizer's 2014 annual report on Form 10-K, and in our reports on Forms 10-Q and 8-K.

We'll now make some prepared remarks, and then we'll move to a Q&A session. With that, I'll now turn the call over to Albert Bourla. Albert?

Albert Bourla - *Pfizer Inc. - Group President Vaccines, Oncology & Consumer Healthcare*

Thank you, Chuck. And good afternoon, everyone. I'm pleased to be here today to provide greater context on Pfizer Oncology, and the strides we have made to further our goal of developing innovative and effective medicines to improve the lives of people living with cancer.

During our remarks, we will provide a brief overview of our Oncology business, coming off a strong presence at ASCO; give an update on how things are going since we launched IBRANCE in the US, earlier in the year; and discuss the positive results from PALOMA-3, our Phase 3 trial for patients with HR+, HER2- metastatic breast cancer, whose disease has progressed following endocrine therapy. We will also provide an update of our investment in immuno-oncology.

Oncology is a critical component of Pfizer's innovative core. We have put significant focus and resources behind building our Oncology business. As a result, we have a growing in-line portfolio, highlighted by four launches since 2011.

As you know, in February, in the US we received approval and launched a first-in-class molecule that has potential to be a new standard of care in breast cancer. We also have an extensive development plan to potentially expand its usage into other tumor types. We have a strong presence in the areas where the science is moving quickly, and where we believe we have clinical differentiation or, more importantly, where the patients' needs are the greatest. Our pipeline includes both late-stage assets and early-stage growth platforms.

For our growing late-stage portfolio, we have 14 Phase 3 trials with nine assets. We are especially excited about additional indications for IBRANCE, and the start of pivotal studies for avelumab, the PD-L1 being co-developed through our alliance with Merck KGaA. In short, we have quickly prioritized up to 20 programs, with up to six of them being registration-enabling trials to begin this year.

For our early-stage pipeline, and beyond avelumab, we have a broad immuno-oncology portfolio across numerous mechanisms, including PD-1, 4-IBB, OX40, a vaccine-based immunotherapy regimen, and CCR2, with more to follow. Of note: No one else has so many immuno-oncology agents simultaneously in development. In addition, we have a strong small molecule pipeline, and a range of antibiotic drug conjugates.

As you're aware, in April we announced that our PALOMA-3 trial was stopped for efficacy, having met its primary endpoint of improving progression-free survival. We will highlight what was shared at ASCO, detailing the efficacy and safety results. In addition, we had several presentations at ASCO, including oral data presentations for our oncology asset, 4-1BB, and avelumab. Mace will provide a more in-depth overview of our approach to immuno-oncology.

I now want to introduce Liz Barrett, our new Head of Pfizer Global Oncology. Liz is responsible for clinical development and commercialization of our assets worldwide. Today, Liz will provide a commercial update on the US launch of IBRANCE. Liz?

Liz Barrett - *Pfizer Inc. - President of Pfizer Oncology*

Thank you, Albert. Good afternoon, everybody. As Albert mentioned, in February we received accelerated approval from the US FDA for IBRANCE, and quickly launched in the US on the same day. In March, shortly after approval, IBRANCE was included in the NCCN guidelines, a testament to the value the product brings in addressing a high unmet need.

While it's still early, I'm extremely pleased with the performance of IBRANCE so far. In Q1, we reported $38 million in sales. And we continue to see uptake, as physicians embrace the product in both the community and academic settings.

Our first-line market share is now approximately 20%, up from about 10% when we last spoke about this in our earnings call in April, while the number of patients and prescribers have also more than doubled since then. We're seeing the number of new patient starts continue to increase since the approval, and there is early success with reimbursement to date.

Over 4,000 patients have initiated therapy on IBRANCE, and over 1,700 physicians have prescribed the product so far. The IBRANCE team has done a remarkable job in collaborating with stakeholders and the cancer community to ensure that patients who need the product are able to access it as quickly as possible, following approval.

In addition, we expect gradual growth over the course of 2015 as IBRANCE gains further acceptance and experience in both the community and academic settings. We look forward to bringing this product to other markets, and plan to make our regulatory submission to the EU later this year.

As Albert mentioned, yesterday we announced the results of our study, PALOMA-3, which was stopped for efficacy, and reinforced the efficacy and safety of the product. This data was accepted as a late-breaker at ASCO, and simultaneously published in the New England Journal of Medicine. The article referenced not only the efficacy and safety of the data, but also the relatively higher quality of life.

With that, I'd now like to turn it over to Mace to discuss the key clinical data that was presented at ASCO on IBRANCE. Mace?

Mace Rothenberg - *Pfizer Inc. - Head of Clinical Development and Medical Affairs & Chief Medical Officer*

Thank you, Liz. Let me start by talking about clinical data that was presented on PALOMA-1, our randomized Phase 2 trial in first-line advanced breast cancer that can further help to define how IBRANCE may be used in a clinical setting.

At ASCO, we reported on four subset analyses from PALOMA-1, which reinforced the safety and superiority of palbociclib plus letrozole versus letrozole alone in post-menopausal women as first-line treatment for advanced breast cancer. Of these data, new insights were shared that could help inform clinical practice.

The subgroups we looked at included women over and under 65 years of age, women with bone metastases as their only site of disease, and women who had not received prior systemic therapy. We also looked at the long-term safety of palbociclib plus letrozole after one and two years. Efficacy benefit was observed across all of these groups, and the safety was consistent with the overall trial population.

I'm now going to discuss our featured data from PALOMA-3, which was received with a lot of excitement yesterday. This is a randomized, controlled, double-blind trial that enrolled 521 women with hormone-positive breast cancer who had already received endocrine therapy and experienced disease progression. Importantly, the PALOMA-3 study population included both pre-menopausal and peri-menopausal women, in addition to post-menopausal women. This represents the first time both populations were included in the same Phase 3 study.

In the study, the combination of palbociclib plus fulvestrant was compared to fulvestrant alone at the 500-milligram dose, which is a current standard of care. The patients in the trial were randomized two to one, with the majority of patients receiving palbociclib plus fulvestrant. The results of PALOMA-3 showed palbociclib in combination with fulvestrant was superior to treatment with fulvestrant alone, significantly extending progression-free survival in women with hormone receptor positive, HER2- negative metastatic breast cancer.

Median progression-free survival in the palbociclib arm was 9.2 months, compared to 3.8 months in the control arm, with a hazard ratio of 0.422. These results are compelling evidence that expands the potential of palbociclib as an innovative first-in-class therapy for women with this type of breast cancer.

From a safety perspective, palbociclib was well tolerated, and the adverse events observed with palbociclib in combination with fulvestrant were consistent with their respective labeled adverse event profiles. The most common adverse events reported for the palbociclib-fulvestrant group were neutropenia, leukopenia, fatigue and nausea.

On neutropenia, the rate of febrile neutropenia was low, 0.6% in both treatment arms. Overall, the low discontinuation rate due to adverse events of only 2.6% reflects that this regimen can be well managed by physicians, and those patients who are benefiting from the drug can remain on therapy.

We have an extensive development program that aims to expand the number of patients that can benefit from this important therapy in breast cancer and beyond. As you can see, the target populations and combinations are designed to address different segments of breast cancer, and substantively improve standard of care.

Our current label for IBRANCE is based on PALOMA-1, which covers the post-menopausal, ER+, HER2- advanced metastatic breast cancer patients who have not received prior endocrine therapy for advanced stage disease. We estimate the addressable population is approximately 50,000 patients in the G7 countries.

The PALOMA-3 study enrolled pre-, peri-, and post-menopausal women with hormone receptor positive, HER2- advanced breast cancer. And we estimate the addressable population in this group to be approximately 65,000 patients in G7.

Going forward, we have a number of additional studies that target different segments of breast cancer patients. For instance, PALOMA-2 is our Phase 3 confirmatory study, and has the same study design as PALOMA-1. Enrollment has been completed, and we expect the study to complete by the end of the year.

PEARL is similar to PALOMA-3, but compares palbociclib plus exemestane to chemotherapy in second- and third-line metastatic breast cancer patients. This study began in March 2014, and is expected to complete in 2018.

PENELOPE-B, another Phase 3 study, is being performed in women with early-stage breast cancer who are at high risk of recurrence. This study began accrual in November of 2014. In addition to breast cancer studies, we're also exploring additional tumor types, such as pancreatic cancer, and head and neck cancer.

Now I will turn it back to Albert to talk about our multi-pronged approach to immuno-oncology. Albert?

Albert Bourla - *Pfizer Inc. - Group President Vaccines, Oncology & Consumer Healthcare*

Thank you, Mace. And very exciting news from PALOMA-3.

Our work in the immuno-oncology space enables us to rapidly identify and evaluate the most promising strategies to develop immune-based therapies to help the most patients. First, we are focused on a single-agent program. We know some patients benefit from single immuno-oncology agent therapy, such as PD-L1 and PD-1 molecules. And we are committed to understanding this more through our program, particularly with avelumab.

Second is our incredible potential with combinations. Given our partnership with Merck KGaA, and the breadth of our portfolios, joined experience and significant resources, this powerful combination uniquely positions us to address areas of significant unmet medical needs.

This year, we have a wide portfolio of known immuno-oncology agents that can play a role in combination, like our ALK/ROS inhibitors and INLYTA, among others. This broad range of combinable agents will allow us to play a leadership role in combination immunotherapy approaches. And we will continue to leverage business development to expand the portfolio, and position Pfizer to be a leader in combinations.

Now, I will turn it again back to Mace to talk about our immuno-oncology pipeline. Mace?

Mace Rothenberg - *Pfizer Inc. - Head of Clinical Development and Medical Affairs & Chief Medical Officer*

Thank you, Albert.

This slide demonstrates the breadth of our immuno-oncology pipeline. We have developed programs that target a variety of tumor-immune mechanisms. These include checkpoint inhibitors, but also extend to other important elements of the immune system, including activators of T-cells, agents that deplete T-regulatory cells, agents that abrogate immune suppression from macrophages and myeloid-derived suppressor cells, an allogeneic approach to chimeric antigen receptor engineered T-cells, or CAR-T cells. We believe Pfizer is well positioned to identify and develop rational combinations that have the potential for significantly differentiated efficacy.

As Albert mentioned earlier, we have a wide-ranging immuno-oncology portfolio of distinct molecules, including six new assets that are, or will be, in clinical development this year, with more to follow. These include PD-1, PD-L1, which is avelumab, 4-1BB agonist, an OX40 agonist, vaccine-based immunotherapy regimen, what we call VBIR, and a CCR2 agonist.

Through our alliance with Merck KGaA, we're using the complementary strengths and pipelines of both organizations, and have the opportunity to broaden the use of IO therapies for patients. We're confidently moving forward with our development plans for avelumab, which is the only PD-L1 supported by the strength of two major pharma companies across a wide spectrum of cancers. We remain on track this year to initiate up to 20 programs, including up to six Phase 3 monotherapy or combination trials for the treatment of non-small cell lung cancer, ovarian, gastric and other solid tumors.

Now turning to ASCO, we presented Phase 3 data from the JAVELIN solid tumor study, also known as the Octopus study because of so many different patient groups included, that enrolled more than 650 patients. This study assessed the safety and efficacy in a subgroup of 184 patients with relapsed non-small cell lung cancer. Avelumab monotherapy showed early and sustained responses as second-line treatment for patients with metastatic non-small cell lung cancer who had progressed after platinum therapy.

In the trial, disease control rate was achieved in 50%, including 24 patients who had a partial response and 1 patient who had a complete response. The overall objective response rate was 13.6%. 37% of patients were alive at 12 months. Based on the data we have seen from this study, we've recently initiated a registrational study in non-small cell lung cancer as part of a larger development program in lung cancer.

We also presented the largest reported data set of patients with ovarian cancer treated with an anti-PD-L1 therapy. It's important to note that this study included a broad group of patients unselected who were heavily pre-treated, and enrolled 75 patients. The disease control rate was 54.7%, which included eight patients who experienced a partial response, with an overall objective response rate of 10.7%.

As a result of these data, ovarian cancer continues to be a key part of our development strategy. From a safety perspective, avelumab demonstrated an acceptable safety profile in a heavily pre-treated population across a range of tumor types that appears to be comparable to those observed with other PD-L1 immune checkpoint inhibitors.

Shifting to other elements of our IO portfolio, I was very pleased to describe the Phase 1 results of our trial of our 4-1BB agonist known as PF-2566 in patients with relapsed non-Hodgkin's lymphoma. As you recall, 4-1BB is a monoclonal antibody that is an agonist of CD-137 -- binds to that. This is a protein receptor expressed in many immune cells.

In this study, patients with relapsed or refractory B-cell non-Hodgkin's lymphoma received four doses of induction rituximab, and then continuous therapy with 4-1BB for up to two years. The overall response rate in the entire cohort of patients in this Phase 1 trial was 21%. But in the smaller subset of patients with refractory follicular lymphoma or mantle cell lymphoma, the response rate was 38.5%. And that included two patients with complete responses, and three patients with partial responses.

Importantly, this regimen demonstrated this promising activity in this difficult-to-treat group, while it also was associated with a very favorable adverse event profile. Other studies of 4-1BB in combination with checkpoint inhibitors are ongoing.

Albert will now share the vision for Pfizer Oncology with key takeaways. Albert?

Albert Bourla - *Pfizer Inc. - Group President Vaccines, Oncology & Consumer Healthcare*

Thank you, Mace. Our vision is to be a leading oncology player across different modalities, as measured by science, patients impacted, reputation and revenue. As I said earlier, Oncology is a critical component of Pfizer's innovative core, and will continue to be a high priority for investments.

We have a healthy base business with three growth platforms. Our near-term focus is accelerating the global launch of IBRANCE, and expanding to other segments of breast cancer and beyond.

We believe we have a winning strategy in immuno-oncology, and plan to initiate up to six registration studies with avelumab this year, as well as develop 4-1BB, OX40, and other assets in our immuno-oncology portfolio. We are uniquely positioned to be a leader in combinations.

Our pipeline of differentiated early-stage assets is a result of innovative science that is amongst the best in the industry, and we will accelerate the programs to bring the most value to patients and, of course, to Pfizer.

I will now turn it back to Chuck, so we can initiate what I believe will be a very informative Q&A.

Chuck Triano - *Pfizer Inc. - SVP of IR*

Thank you, Albert. Operator, can we now please poll for questions?

QUESTIONS AND ANSWERS

Operator

(Operator Instructions)

Your first question comes from the line of Mark Schoenebaum from Evercore ISI.

Vlad Nikolenko - *Evercore ISI - Analyst*

This is Vlad Nikolenko on behalf of Mark today. The biggest question that investors on our side keep asking us, it looks like the next generation of immuno-oncology treatments will be based on combinations. Pfizer already highlighted a few combinations with 4-1BB. And the question is, what would differentiate programs that are started by Pfizer, or about to be started in clinics, specifically for combination treatments, either with internally developed assets, OX40 or4-1BB, or potentially in license.

And a second quick question, should we expect PALOMA-2 overall survival data this year, just to confirm that? Thank you.

Albert Bourla - *Pfizer Inc. - Group President Vaccines, Oncology & Consumer Healthcare*

Thank you, Vlad. Let me take the PALOMA-2 and then I will pass to Mace so that he can speak about the differentiation we can have in the oncology space.

For PALOMA-2, as you know it's event driven. We have completed enrollment but it is event driven. Right now we expect that we will come to primary completion at the end of the year, which means that the readout will be in first quarter of next year.

With that, Mace, can you please handle the question about how we will differentiate in this space, immuno-oncology space.

Mace Rothenberg - *Pfizer Inc. - Head of Clinical Development and Medical Affairs & Chief Medical Officer*

What we can say is we're very excited about the activity that we've observed with immuno-oncology agents like avelumab. It is clear that this is a category of drugs that is fundamentally going to change the way that we treat cancer in the future. It's not going to replace all the existing therapy. Most likely it's going to be used in conjunction with that.

If our lessons of the past have any relevance to the future, what we know is that using anti-cancer drugs in combination is far superior to using them as single agents. And I think that same lesson holds true for immuno-oncology agents. It's really up to us, and we believe we'll become a leader in this field, to understand what the best combinations might be.

That could include combining immuno-oncology agents with other immuno-oncology agents, combining IO agents with antibody drug conjugates, combining IO agents with small molecule inhibitors. There are almost an innumerable number of possibilities. And it's really up to us to make sure that we approach this with keen insight into the biology, and understanding which are going to be the most productive and successful combinations.

Having said that, we think that we are uniquely positioned with a number of agents across all of these platforms, including CAR-T cells, to be able to be among the leaders in identifying the most promising and active combination regimen.

Operator

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

Chris Schott - *JPMorgan - Analyst*

Great. Thanks very much. First of all, on Ibrance, can you just elaborate a little bit more on the second-line opportunity? Specifically, how quickly can we think about the ramp of this product given the fairly large diagnosed population here? Should we think about this rapid uptick we've seen in first line as a decent proxy for what second line could look like?

And then my second question is just coming back to the competitiveness of avelumab versus some of the other PD-1 and PD-L1 molecules we're seeing out there. It seems like some of your early lung data here is modestly below that of your competitors. Is there a difference in patient populations we should think about here? Or just any perspective you might have. I know you guys are very excited about the combo opportunity, et cetera, but I'm just trying to understand the molecule itself, your conviction that this is a competitive molecule you have. Thanks.

Albert Bourla - *Pfizer Inc. - Group President Vaccines, Oncology & Consumer Healthcare*

Thank you, Chris. I think Liz can speak about the Ibrance second-line opportunity, once the product is approved, of course.

Liz Barrett - *Pfizer Inc. - President of Pfizer Oncology*

I think the question is around approval and we're obviously working very closely with the FDA to seek an expansion of the label inclusive of this new data. I think in the US, as you know, do we expect that there may you be some uptake? -- Yes. I think that there is likely to be not at this same level that we've seen in first line because there won't be an indication. I think it will depend on the ability to get reimbursed. But I suspect that some physicians will use it given the data that they've seen, the very compelling data and, frankly, the enthusiasm that they've shared with us around this data. We clearly, obviously, would like to focus on first line and that's what we'll be focused on, as that's our current indication.

Albert Bourla - *Pfizer Inc. - Group President Vaccines, Oncology & Consumer Healthcare*

Thank you very much, Liz. Mace, what about avelumab and how competitive it is versus the other PD-L1s, PD-1s?

Mace Rothenberg - *Pfizer Inc. - Head of Clinical Development and Medical Affairs & Chief Medical Officer*

We're still at very early stages of understanding how best to capture and qualify and quantitate the anti-tumor effect of these immune-targeted agents. We have used objective response rate which, remember, was developed in the era of cytotoxic chemotherapy. When we look at it now, we never expected to see tumors get bigger before they got smaller because that never happened with cytotoxic agents, and it's happening with IO agents. So, I think we have to look beyond the response rate element.

And, actually, when you look across other PD-1 and PD-L1 inhibitors, the disease control rate and the one-year survival rates from our 184-patient experience in second line is very consistent with those reported for other agents. And remember, it's very difficult to compare across trials because we have different patients populations, different distributions. And we're beginning to realize how those baseline patient characteristics could also influence the anti-tumor effect that's observed. From my perspective, I think that what we've seen out of avelumab is perfectly consistent with other PD-1 and PD-L1 agents, and it's going to be very competitive in that space.

Operator

The next question comes from the line of Tim Anderson with Bernstein.

Tim Anderson - *Bernstein - Analyst*

Thank you. I'm wondering if you can tell us what your thinking is about combining PD therapy with chemotherapy. Are you more in the Bristol camp where they don't seem to think there is much of a benefit in adding them together, or are you more in the Roche camp where they think there's a big benefit? And do you have any data with avelumab in combination with chemo that guides any opinion you have?

And then on 4-1BB, you signed a partnership with Merck to combine 4-1BB with their PD-1 early last year, and then late last year you signed a broad agreement with Merck KGaA. In principle you don't need Merck as a partner anymore. What should we expect about the status of that relationship going forward and that agreement with the US-based Merck?

Albert Bourla - *Pfizer Inc. - Group President Vaccines, Oncology & Consumer Healthcare*

Yes, thank you. I can take the last one and then I will give it to Mace so he can speak. The partnership with Merck KGaA involves combination with their PD-L1 of multiple assets that we have or they have, and includes also PD-1, what we have as part of the overall alliance. The study what we had with Merck in the US with PD-1 and now 4-1BB will continue and we will both serve the results.

With that, Mace will tell us, which camp. We are actually on the Pfizer camp, but he will tell you how this camp thinks about it.

Mace Rothenberg - *Pfizer Inc. - Head of Clinical Development and Medical Affairs & Chief Medical Officer*

I think I can best describe our position as agnostic on that point. I think we have no data available to share with avelumab and chemotherapy. Our approach is going to be to combine avelumab with the agent or agents where we get the most increased effect with a tolerable side effect profile. So, I think going in with that agnostic approach will position us to find the best one and move that forward.

Operator

The next question comes from the line of Alex Arfaei with BMO Capital Markets.

Alex Arfaei - *BMO Capital Markets - Analyst*

Great. Thank you for taking the question and congratulations on the early Ibrance launch. Mace, a question on Ibrance. And thank you for providing the addressable patient numbers for PALOMA-1 AND PALOMA-3. But could you also do the same for PENELOPE? What is the addressable market size that we're looking at, patient population?

You showed very nice data with 4-1BB and with Rituxan. Could you give us more details about the development plan, specifically by tumor type and approximate timing as to when we can expect data? And, also, when can we see data for OX40? Thank you.

Mace Rothenberg - *Pfizer Inc. - Head of Clinical Development and Medical Affairs & Chief Medical Officer*

Okay. Let me start with -- the first question was?

Albert Bourla - *Pfizer Inc. - Group President Vaccines, Oncology & Consumer Healthcare*

It was around the patient population. And maybe I can cover it briefly before Mace answers. As you know, globally, the breast cancer new cases is 1.7 million every year and 60% of them they are ER+/ HER2-, so let's say 1 million, approximately, new cases every year. And approximately 45% of that, 450,000 cases, it is in the G7 of that. This G7 includes the overall with a potential of Ibrance if we develop for the entire population.

Right now we are, as Mace said, in the first 50,000 that we have for first line, and then we are developing for the remaining of that. That includes 60,000, 65,000 patients, but they're in recurrent mode. And then, of course, there is the early breast cancer which is a much bigger population to come all the way to this 450,000 patients, approximate.

As I said, these are approximate numbers. And also the different status that are evolving are covering different parts of this population. So, with that, I will ask Mace to take the 4-1BB question.

Mace Rothenberg - *Pfizer Inc. - Head of Clinical Development and Medical Affairs & Chief Medical Officer*

This is the first report of our experience with our 4-1BB agonist, PF-2566 in Rituxan. And it was done specifically in the refractory group of patients with non-Hodgkin's lymphoma. So, it's taken a while to accrue these patients and also, as you know, there are many subgroups of non-Hodgkin's lymphoma.

As you know, some of these subgroups, like follicular lymphomas, can be responsive to a number of therapies, and there are some recently approved drugs in this space. So, it took a little while for us to be able to see do we have something here that might be exciting. As time passed and we realized the depth and duration of some of the responses we were seeing, especially in the follicular lymphoma, and mantle cell lymphoma groups, the answer emerged as a clear yes.

For instance, in that cohort of patients, we have two complete responses. This is complete responses in Rituxan refractory patients. What makes it even more interesting and exciting to me is that both these patients had completed therapy and are still in CR a year and a half after completing that therapy. So, these are durable, as well.

What also impresses me is the very low rate of grade 3 and absence of grade 4 adverse events with this combination, which is in stark contrast to some of the other therapeutic options in this group of patients. So, this is really new information, it's emerging, and we are going to be moving very quickly to follow up on this.

And then lastly, the OX40, we just dosed our first patient. It's way too early to say anything about that. But, again, very excited to have reached this point.

Operator

Your next question comes from the line of Vamil Divan with Credit Suisse.

Vamil Divan - *Credit Suisse - Analyst*

Great. Thanks so much for taking the questions. Two questions, please. One just on the biomarker strategy, if you can clarify a little bit more your views there post ASCO. Obviously a lot of discussion there around PD-L1 as a biomarker and how you guys are thinking about that at this point,

the importance of that as a biomarker. And maybe if you can expand on other efforts you may be making on the biomarker front in terms of gene expression signatures or other approaches to try and help select patients properly.

And then the second one you mentioned, you obviously have a PD-L1 and then PD-1, as well. If you could maybe just talk a little bit about any differences you see between the two approaches, if there's different indications that you may be pursuing, or is it maybe more of a matter that one is part of the collaboration and one is not and that could dictate how you develop the two different assets. Thanks.

Albert Bourla - *Pfizer Inc. - Group President Vaccines, Oncology & Consumer Healthcare*

Yes. Thank you very much, Vamil. I think Mace is uniquely positioned to answer both our view on the biomarker strategy and also the PD-L1 and PD-1, are there any differences. As I said, in terms of our agreements with Merck KGaA, both molecules are part of the alliance so both companies will develop them and benefit from this development. Mace?

Mace Rothenberg - *Pfizer Inc. - Head of Clinical Development and Medical Affairs & Chief Medical Officer*

Thanks, Vamil. I think the biomarker strategy is one that we're realizing is going to be more challenging than simply the PD-L1 expression in tumors. Number one, because we're using different cut points. Number two, we're using different assays. Number three, in different settings it may have greater or lesser association with sensitivity -- namely, if you use a PD-1 or PD-L1 as a single agent or in combination.

The approach that's being taken in the ongoing second-line non-small cell lung cancer study is to take all comers, but to collect samples from those patients and analyze them for PD-L1. The primary analysis is going to be done in that group of patients. So, I think that that's going to be important. It's being able to leverage and build off of our current level of knowledge and understanding but at the same time in those samples that we obtain we also are going to be analyzing them for gene expression. We don't have all the details worked out yet, but clearly I think this discussion a year or two years from now we'll be discussing more than just PD-L1 expression.

The differentiator between the PD-L1 and PD-1, right now it's somewhat subtle. It may be somewhat different frequencies or severities of adverse events. But I think with more exploration and development of these agents, there may be situations where one category proves to be more appropriate than another.

Years ago, I was involved in the development of anti-EGFR agents. And if you asked me at that time in the early days whether there would be a difference between a small molecule inhibitor versus a monoclonal antibody I would tell you no, except one's easier to give because one's a pill and one's an injection. And we know how that story played out, how each has a very distinct and very important role to play in different diseases.

So, given where we are right now in this field, I cannot rule out the fact that there may not be some differentiation between these two classes of agents.

Operator

Your next question comes from the line of Seamus Fernandez with Leerink.

Seamus Fernandez - *Leerink Partners - Analyst*

Thanks very much. Just a couple quick questions. First off, on the PD-L1 test that was utilized, we saw 89% PD-L1 positivity. That implies a fairly low level of specificity. Just wondering if you are pursuing other PD-L1 testing metrics to basically get this to be a more selective biomarker overall.

Second, on Ibrance, can you just help us understand how you think Ibrance can actually be used in the real world setting? You now have an indication in combination with aromatase inhibitors in the front-line setting and an indication now with fulvestrant in second line setting. How do

you expect physicians to actually use Ibrance? Is it possible that this could suggest continuous dosing? Or do you have to prove that and so these will be bucketed patient populations rather than even a continuous patient population?

And then, lastly, as we think about the adjuvant setting, the safety of Ibrance, can you just help us understand how the neutropenia that continues to be seen could be managed, particularly given the very long duration of treatment that's associated with this? Thanks a lot.

Albert Bourla - *Pfizer Inc. - Group President Vaccines, Oncology & Consumer Healthcare*

Thank you, Seamus. All three excellent questions and they are all very medical questions, so I think Mace is the appropriate person to answer again.

Mace Rothenberg - *Pfizer Inc. - Head of Clinical Development and Medical Affairs & Chief Medical Officer*

Okay. Thank you, Seamus. Starting with the first one, the PD-L1 test, that is the Dako test that's being used. And, as I mentioned, we're still at very early stages of trying to understand the best way of utilizing these tests. As you know, each sponsor of PD-1 or PD-L1 has its own proprietary test so the comparability across studies and across molecules is really challenging.

I think that, as I mentioned earlier, working with Merck KGaA and Dako, we're going to be trying to understand how we might be able to make this more rigorous. But we're not at a point to say right now exactly what steps will be taken, so stay tuned for that.

With regard to the Ibrance, yes, the PALOMA-1 and PALOMA-2 have combined Ibrance with letrozole or Femara. And that has and will be generating additional data in the first-line metastatic setting in women who are hormone-therapy naive. The PALOMA-3 is in hormone previously treated women who have progressed, and there we have data with fulvestrant.

As a sponsor, really, what we have to adhere to is what the data has shown, the activity of Ibrance in those settings with those partners. Clearly we are conducting studies. As I mentioned the PEARL study combines Ibrance with exemestane. There are other investigator initiated studies that are combining with other aromatase inhibitors that will be generating data. But this is really for those studies to be able to address in terms of the experience with the different anti-estrogen therapies.

Lastly, with regard to safety, this is something that's I think very important to us and investigators and to potential study subjects. Any drug that's brought into the early-stage setting where the patients may already have been cured by prior therapy, and were looking to improve that cure rate, has to have a very favorable benefit/risk relationship. It has to have a favorable adverse event profile that allows the drug to be administered at or close to the full dose for the entire duration. We think that Ibrance meets those criteria.

Remember that in PALOMA-3, even though there was the incidence of neutropenia that you've mentioned, only 2.6% of women had to discontinue therapy due to an adverse event. That's extraordinarily low. And even though the incidence of neutropenia is on the high side, above 50%, keep in mind two things. Number one, the incidence of grade 4 neutropenia is only 9%, so it's relatively infrequent. Number two, the incidence of neutropenic fevers was low at only 0.6%. And, number three -- actually I have more than two -- number three is that we have a very well-managed ability to dose reduce or interrupt dosing during the treatment cycle to allow the patients to recover and then restart the drug either at the same dose or at a lower dose -- really, a system that's been developed to allow women who are benefiting from Ibrance to continue on Ibrance.

Lastly, let me point out that the mechanism of neutropenia is different than the mechanism of neutropenia with cytotoxics. We are not damaging and killing neutrophil precursors. We are stopping them temporarily in the cell cycle. As soon as that drug comes off, those neutrophil precursors are able to continue in their cell cycle and push out new neutrophils. So, we think that's one of the reasons why, despite the incidence of neutropenia, we're seeing such a low incidence of neutropenic fevers or infections.

Operator

Your last question comes from the line of Marc Goodman with UBS.

Ami Fadia - *UBS - Analyst*

Hi, this is Ami Fadia on behalf of Marc Goodman. We have one question on the PALLAS study. Could you elaborate a little bit on it and give us a sense of what type of patients you would be targeting in that study, and how that fits into the broader development plan for the product? Thanks.

Mace Rothenberg - *Pfizer Inc. - Head of Clinical Development and Medical Affairs & Chief Medical Officer*

Thanks, Ami. Let me start with the other study we're doing now in the early-stage space and that's PENELOPE-B with the German Breast Group. That is for a group of women who received neo-adjuvant chemotherapy and radiation before surgery, and because of some certain characteristics in their tumor are at fairly high risk of recurrence.

We realized this population accounts for only about 5% or 10% of women with early stage ER+ breast cancer. We realize that there is also a potential benefit, as we got more information, more data about the tolerability of Ibrance, we recognize that there's a larger addressable population, a group who have intermediate or high risk of recurrence and using this in women who did not get neo-adjuvant therapy.

We're now working with some major international cooperative groups on finalizing the design of that study and finalizing the details, so that there will be additional information coming up soon about specific details about eligibility, sites, centers, trial design, et cetera. So, stay tuned for that.

Albert Bourla - *Pfizer Inc. - Group President Vaccines, Oncology & Consumer Healthcare*

But very excited about PALLAS because it's the next step in developing palbociclib. So, very excited.

Chuck Triano - *Pfizer Inc. - SVP of IR*

Thank you both. Thank you, everybody, for your attention this afternoon.

Operator

This concludes today's conference call. You may now disconnect.