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PFE - Pfizer Inc at Leerink Partners Immuno-Oncology Roundtable

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Chris Boshoff *Pfizer Inc. - VP, Early Development, Translational and Immuno-Oncology*

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Seamus Fernandez *Leerink Partners - Analyst*

PRESENTATION

Seamus Fernandez - *Leerink Partners - Analyst*

Okay, thanks, everybody. And thank you for joining us at our inaugural Leerink Partners Immuno-Oncology Roundtable. This is a really exciting space and I am particularly pleased to be able to turn the mic over to Pfizer. We are joined by Liz Barrett, President and General Manager of Oncology, and also Chris Boshoff, the VP of Early Development, Translational and Immuno-Oncology.

So with that, I will turn it over to Liz and they will kick off their presentation.

Liz Barrett - *Pfizer Inc. - President, General Manager of Oncology*

Thank you, Seamus, and good morning, everyone. Thank you for having us here. As said, I am Liz Barrett and I head up the global business for Pfizer. And I am pleased to introduce you to our immuno-oncology portfolio, and Chris will really take you through a lot of the details.

I want to first do the obligatory forward-looking statement disclosure, so here it is; I won't read it to you. I am sure you have seen it many times.

So this next slide is a busy slide and I promise I won't go through it in detail, but it is a good overview of our strategy for Oncology. Oncology is a critical component of Pfizer's Innovative core. We have really put a lot of focus and investment behind Oncology and as a result, have launched four products in the last four years. So our pipeline includes both late-stage and early-stage growth platforms.

So for our growing late-stage platform, as you can see here, we have 14 Phase 3 trials across nine assets. We are especially excited about the partnership that we have with Merck KGaA, which you will hear more about with avelumab, our PD-1 inhibitor that Chris will take you in -- talk to you more in detail about in a moment.

For our early-stage portfolio, we have a broad range of immuno-oncology molecules across many mechanisms. We also have a strong small molecule pipeline and a range of ADCs or antibody drug conjugates, and we'll hear a little bit about that.

So in February in the US we received approval and launched Ibrance, a first-in-class molecule that we expect to be the next standard of care in breast cancer. So in addition, as you can see at the bottom, we have a comprehensive development plan across all breast cancer populations as well as non-breast tumors.

So on the right-hand side you will see we are taking a comprehensive approach to immuno-oncology. And like I said, Chris will talk to you more about that. We think it is really important that you target the immune system across many multiple mechanisms, as you actually heard this morning from Seamus' presentation.

And lastly on this slide, what we are showing here at the bottom is that we have several technologies in our early discovery engine to ensure that we remain on the leading edge of innovation for the future.

So we are really excited about both the near-term and long-term prospects of Pfizer Oncology. Our palbociclib, Ibrance launch is exceeding expectations. We plan to deliver one to two new launches a year. Seven to nine pivotal studies will start this year, and we expect three to five pivotal studies each year for the next three years.

So we believe Pfizer is uniquely positioned to win in immuno-oncology with our broad portfolio and our unique combinations. And I will introduce Chris Boshoff who will take you through the details of that portfolio. So, Chris.

Chris Boshoff - *Pfizer Inc. - VP, Early Development, Translational and Immuno-Oncology*

Thank you very much, Liz. Thank you for giving me the opportunity. So essentially our immuno-oncology strategy and approach, this is based on three pillars. First the development of a single-agent program mainly focused on avelumab, and I will expand on that.

Then combinations; these are combinations with Pfizer in-house and immuno-oncology compounds, as well as some of our antibody drug conjugates and other small molecules. And I'll expand a little bit upon that.

And then lastly of course through business development, we want to continue to use business development to increase the footprint of Pfizer Immuno-Oncology. And I just highlight two of the recent agreements, that with a CAR-T cell program with Cellectis, an allogeneic approach, and as well as our IDO1 program with iTEOS.

And as Liz pointed out, we now have a number of molecules that really target or that potentially could target various aspects of the immune landscape of cancer. So of course we are all aware of our 4-1BB that is currently in the clinic. This is an agonist of the immune system. This stimulates preferentially CD8 positive T lymphocytes.

We also have an OX40 currently in the clinic. This is again an agonist antibody stimulating the immune system, perhaps more so CD4 positive T lymphocytes. So the potential to combine 4-1BB and OX40 for the future and, of course, preclinical data supporting that combination strongly.

Then our checkpoint inhibitor program, the agreement -- the co-development program with Merck KGaA for avelumab, as well as our own anti-PD-1 that will enter the clinic soon. And I will say more about -- I will expand more on avelumab and the program being planned and the current clinical studies.

We do have an agreement with KHK for collaboration to use their CCR4 antibody mogamulizumab in combination with 4-1BB, and that study is currently in -- is currently ongoing. As we know, certain cancers do not respond to checkpoint inhibitors because the immune system is dampened by so-called T regulatory cells. And mogamulizumab is particularly well-suited to deplete T regulatory cells and, therefore, can be used in combination with other compounds then again.

We also have molecules in development and currently in the clinic to target myeloid-derived suppressor cells. Myeloid-derived suppressor cells, of course another type of cell type that dampen the immune response. M-CSF currently in Phase 1 with MD Anderson, a CCR2 inhibitor that is already presented -- that was previously presented this year at ASCO GI in combination with cytotoxic therapy in pancreatic cancer, as well as our IDO1 program that is currently in preclinical development. And then lastly, the CAR-T cell program I mentioned.

So one of our pillars is certainly combinations, and this is just a summary slide of some of the combinations now currently ongoing in the clinic or that are planned that will start shortly in the clinic.

Avelumab already, if we look at this slide, is emerging as an anchor molecule for many of these combinations, not only with other immunotherapeutics but also with our ADC program and with some of our small molecules. For example, with Inlyta in renal cell cancer, a study that will start shortly.

And of course as Liz mentioned, Ibrance is emerging as an anchor molecule within our portfolio that is already being used with various combinations, both in breast cancer and being explored outside of breast cancer.

So avelumab is an IgG1 human antibody. It is not engineered, so it is slightly different from the competitor molecules durvalumab or the other molecules in this class, durvalumab and atezolizumab. It is not engineered. It can, therefore, engage the Fc gamma receptor and elicit potentially so-called antibody mediated cellular cytotoxicity.

If there is time during the discussion or afterwards, we can perhaps allude more to the potential differential effects of this antibody because of this effect that is seen preclinically by eliciting ADCCs.

So this is the clinical program for avelumab. The program is called JAVELIN program. Importantly, over 1,200 patients have now been treated across 15 different tumor types with avelumab. We have completed efficacy cohorts and these are approximately 150 patient cohorts for gastric cancer, non-small cell lung cancer, metastatic breast cancer, as well as head and neck cancers. And these will form the basis for some of our registration studies to be launched.

We have completed signal detection studies and ongoing expanse in efficacy cohorts. That is also the basis for future combination studies and for some of the randomized trials and pivotal studies that is planned.

And for the first time, we reveal the whole program as it currently stands and also the Phase 3 and pivotal studies that should start very shortly in the next -- now or in the next couple of months. So in red, the Phase 1 studies, the ongoing studies. Most of these have now completed recruitment and the patients are currently being followed up.

Merkel cell carcinoma Phase 2 study has now completed recruitment, and this is currently the largest cohort of any checkpoint inhibitor and treated for Merkel cell carcinoma. This was in second-line setting.

And then we have an ongoing pivotal study in non-small cell lung cancer in the second-line study -- in the second-line setting that is recruiting well and that is on track.

Combination studies that will start very shortly, our own molecule Inlyta axitinib, axitinib plus avelumab. The registration study will follow shortly after a short Phase 1 study. This is avelumab plus Inlyta versus Pfizer's Sutent in first-line renal cell carcinoma.

Avelumab plus Xalkori and avelumab plus the next generation ALK inhibitor, potentially best-in-class, lorlatinib. That will start very shortly and it will be followed by a randomized pivotal study in the first line setting of ALK positive non-small cell lung cancer.

Avelumab plus 4-1BB in non-small cell lung cancer, head and neck cancer, and in melanoma. A number of registration studies starting now with avelumab monotherapy, Merkel cell carcinoma first line, non-small cell lung cancer first line, head and neck cancer second line, and Hodgkin's lymphoma Phase 1 study.

And in combination registration studies, and that is currently being finalized to start within the next couple of months. Bladder cancer first line, this is with chemotherapy -- with sequential therapy with chemotherapy; gastric first line; gastric third line; ovarian cancer platinum resistant refractory disease, this is with doxil -- doxil versus avelumab plus, doxil versus avelumab; and ovarian platinum sensitive first line with chemotherapy.

I will just end up to highlight 4-1BB. There is currently one other 4-1BB molecule in the clinic, urelumab from BMS. Ours is an IgG2; urelumab is an IgG4. As I pointed out, 4-1BB is an agonist of the immune system; it activates the immune system. And pre-clinical data are compelling for combining a checkpoint inhibitor with an agonist like 4-1BB.

We have ongoing clinic and clinical trials combination studies with 4-1BB, including 4-1BB plus Keytruda, 4-1BB plus Rituxan, 4-1BB plus mogamulizumab. And these are data we recently presented in an oral presentation at ASCO where we've seen significant or very encouraging responses with 4-1BB plus and Rituxan in individuals with follicular lymphoma that is resistant to multiple lines of previous therapy.

As is shown, this individual is now in complete remission for over two years after completing 4-1BB and previously had many, many standard of care therapies for follicular lymphoma, including Idelalisib and Rituxan combinations. Thank you very much.

QUESTIONS AND ANSWERS

Seamus Fernandez - *Leerink Partners - Analyst*

Great, thanks so much, Chris and Liz, for joining us. A couple things just to maybe start off on. On the second-quarter conference call, Ian Read highlighted seven targets for IO development and combinations. You have just talked about a lot of those here. Obviously, there is an emphasis on combination therapy.

But if you were going to kind of focus us down to one or two combinations, maybe three max, which would those be? Because there's obviously a lot of cytotoxic chemotherapy combinations that are also different based on lines of therapy, so there are a lot of differences there. So I think it would help to just kind of guide us in the direction of, if nothing else, where do you see important data coming and the areas that you are excited about?

Chris Boshoff - *Pfizer Inc. - VP, Early Development, Translational and Immuno-Oncology*

So I think the first group will be any combination we are doing with 4-1BB, including the combination with 4-1BB and avelumab. And the data readout we should get early next year on 4-1BB plus Keytruda and the other ongoing studies combinations with 4-1BB. So that is certainly an important area for us.

And our combination study of avelumab and Inlyta, Inlyta already approved compound in renal cancer. So that combination is a rational combination to take into the clinic in renal cancer. So we are looking forward to start that registration study with Inlyta and avelumab in first-line renal cancer against Sutent.

Seamus Fernandez - *Leerink Partners - Analyst*

Great. And can you talk a little bit more about the 4-1BB antibody? There is, I think, some differentiation on the side-effect profile, or there may be differentiation I think. Can you talk about why Pfizer thinks that their 4-1BB is differentiated from urelumab?

Chris Boshoff - *Pfizer Inc. - VP, Early Development, Translational and Immuno-Oncology*

So I can't comment on the adverse event profile of urelumab, the BMS compound. What I can say is for the Pfizer compound across various dose levels, we have got a very manageable adverse event profile. And in the combination studies, as already undergoing with mogamulizumab and with other compounds, it is clearly -- it is a manageable profile for us to use.

The differences, as I point out, is ours is an IgG2, and urelumab is an IgG4. And apart from that, our molecule does not block -- sorry, our molecule blocks the ligand binding to the receptor where urelumab doesn't. So maybe that is different. But we can't speculate what is the reason for the differences.

Seamus Fernandez - *Leerink Partners - Analyst*

Okay. And is it -- in terms of the level of agonism, how do you actually measure that? What is actually being demonstrated? How are you confident that you're actually really agonizing the immune system and upregulating it?

Chris Boshoff - *Pfizer Inc. - VP, Early Development, Translational and Immuno-Oncology*

That is a good question. So we obviously have now clinical data to show efficacy. We have got single-agent efficacy data with 4-1BB in melanoma as well as in Merkel cell carcinoma; and now very nice or encouraging combination studies with rituximab. So efficacy we have now seen.

And we have got a very comprehensive biomarker program with 4-1BB with the re-biopsies built into the program. For example, we have seen expansion of T cell clones -- using NGS, next-generation sequencing, to look at T cell receptor repertoire. And we have demonstrated that in the clinic, which is one of the signs of immune activation.

Seamus Fernandez - *Leerink Partners - Analyst*

Great, and maybe we can talk a little bit about the OX40 antibody. How is your approach different from either Genentech or Astra, or at least what exactly is your approach? And I think one perplexing dynamic is AstraZeneca has three separate antibodies actually in the clinic, one being a murine antibody in humans -- I'm still trying --.

Chris Boshoff - *Pfizer Inc. - VP, Early Development, Translational and Immuno-Oncology*

(Multiple speakers) human antibody. Currently -- perhaps the only thing I can say at this stage is our molecule is currently in Phase 1 in dose escalation. But we are looking forward to start very early on next year with combination studies, including combination with avelumab.

There's preclinical data suggesting that a combination of a checkpoint inhibitor plus 4-1BB plus OX40 could be a rational combination, because you stimulate various arms of the immune system as well as taking off the brake. So we are currently the only company that has all three molecules within our portfolio: OX40, 4-1BB and avelumab. So that is certainly something to look forward to as a potential triplet for the future.

Chris Boshoff - *Pfizer Inc. - VP, Early Development, Translational and Immuno-Oncology*

And I think you guys also have an IDO1 in development as well?

Chris Boshoff - *Pfizer Inc. - VP, Early Development, Translational and Immuno-Oncology*

That is currently in preclinical development; that is correct, yes.

Seamus Fernandez - *Leerink Partners - Analyst*

Okay, great, so that is in preclinical development. When might that enter the clinic?

Chris Boshoff - *Pfizer Inc. - VP, Early Development, Translational and Immuno-Oncology*

We currently haven't declared a date yet for the --.

Seamus Fernandez - *Leerink Partners - Analyst*

Okay, great. You know, Liz, I think one of the things that we talked about earlier today is actually your job is going to be managing the costs to some degree in the business. And we went through that iterative conversation around the number of targets that can be explored.

How are you managing that, and what is the threshold for the types of signals that you really want to see to allow Chris to advance more stuff into the clinic?

Liz Barrett - *Pfizer Inc. - President, General Manager of Oncology*

No, I think that it is a good question, and I think you have been reading a lot about it, right? It has been in the press quite a bit and you showed some numbers earlier. And it is actually one of the reasons why we think we are in a unique position because we do have all of those. So we can in some respects be able to work with stakeholders about how do you price these combinations in the future.

I think the important thing for us, we haven't -- we are embarking on what does that look like for the future, so we actually haven't made any decisions there. But we are not going to let price determine what we do in the clinic because we believe we can manage that once it gets to the market.

I think the important thing for us to find out is which combinations are the right combinations, and are they doublets, are they triplets. And we really believe that we need to -- if it is triplet therapy, you can go from a 30% with a monotherapy to a 50% with a doublet. And if you can get a 70% to 80% response rate, we would want to do that.

So -- and then we would take that challenge on in how we bring it to market and how we are able to work with payers to figure out the best way to price that.

Seamus Fernandez - *Leerink Partners - Analyst*

Great. Let me just see if there are any questions in the audience for a final question. I think we have about one minute left. Okay, I don't see any hands going up, so I will continue.

In terms of, again, maybe just focusing in on the JAVELIN study itself, your second-line lung cancer program with avelumab, the primary endpoint is overall survival. And I am just trying to get an understanding of how that is achievable once Opdivo is broadly available in the US and Europe.

Chris Boshoff - *Pfizer Inc. - VP, Early Development, Translational and Immuno-Oncology*

So obviously, it is only available in certain regions currently. So we are keeping a very close eye on that and do not open the study in sites where we believe avelumab will -- nivolumab will become available. And so far, the recruitment is going well and we are on track. And there is obviously many, many regions in the world where nivolumab is not going to be available for a long time.

Seamus Fernandez - *Leerink Partners - Analyst*

Okay, great. And maybe just as a final question, chemotherapy and chemotherapy combinations; how are you are approaching that?

Chris Boshoff - *Pfizer Inc. - VP, Early Development, Translational and Immuno-Oncology*

So we are -- so as you know, there are certain cytotoxics that has been shown, at least in preclinical models, to elicit so-called immunogenic cell death where chemotherapy come in and kill the cells in a way where they elicit an immune response, so they cause T cells to go into the tumor. One of those compounds is, for example, Doxil.

So we are using Doxil in combination with avelumab in ovarian cancer. And some of our other programs is more sequencing where we give chemotherapy upfront. For example, in our first-line bladder cancer study, four cycles of chemotherapy followed. So it's a sequencing of avelumab or placebo or standard of care.

Seamus Fernandez - *Leerink Partners - Analyst*

Okay, great. Well, it is obviously exciting and very busy times at Pfizer in oncology. Thank you both for joining us here today, and we look forward to continued studies and advancements.

Liz Barrett - *Pfizer Inc. - President, General Manager of Oncology*

Great, thanks, Seamus.

Chris Boshoff - *Pfizer Inc. - VP, Early Development, Translational and Immuno-Oncology*

Thank you.
