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PFE - Pfizer Inc at Leerink Partners Roundtable Series: Rare Disease & Immuno-Oncology

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PRESENTATION

Seamus Christopher Fernandez - *Leerink Partners LLC, Research Division - MD, Major Pharmaceuticals and Biotechnology*

Okay. Thanks, everybody, and thanks for joining us here today. I'm really pleased to be joined by Pfizer and their oncology team. With us today on my far left is Liz Barrett, the Global Head of Oncology; and just to my left is Chris Boshoff, the Head of I/O Early Development and Translational Oncology; and in the audience, we have Chuck Triano. Many of you know Chuck.

But with that, I think I have to turn it over to Liz just to quickly talk through disclaimers, and then we'll jump right into Q&A.

Elizabeth Barrett - *Pfizer Inc. - Global President, Oncology*

Thanks, Seamus. I was told by my legal group, I had to do this. And while Chuck knows this by heart, I'm going to read it to make sure I don't get myself in trouble.

So before we start, I'd like to remind you that this discussion will include forward-looking statements and that actual plans and results could differ materially from those expressed or implied within the forward-looking statements. Factors that could cause actual results to differ are discussed in Pfizer's SEC filings.

So thank you, and we look forward to the discussion.

QUESTIONS AND ANSWERS

Seamus Christopher Fernandez - *Leerink Partners LLC, Research Division - MD, Major Pharmaceuticals and Biotechnology*

Great. So Liz, maybe just from a big-picture perspective, to start off, let's -- maybe give us a sense of how you're seeing the Pfizer Oncology group continue to develop. Obviously, building around Ibrance is a very big focus for the business, but other areas that you're uniquely excited about that you think people might be missing.

Elizabeth Barrett - *Pfizer Inc. - Global President, Oncology*

It's a great question. And I joined Pfizer in 2010, and at that point, we were about $1 billion revenue and had 2 medicines on the market. I think as I -- in the first half of the year, their projections were getting around $3 billion for the first 6 months. So you can sort of do the math yourself. We have 10 medicines now, marketed medicines, and actually expect to introduce 3 new ones in 2018. So you can see the difference in the evolution, and it's really a direct result of the investment that Pfizer has made and the commitment that they made to over-index on oncology in our portfolio and R&D, frankly. And we've spent a significant amount of investment in R&D, and we're starting to see that play out. To your point, we look at our Ibrance franchise as really entrenching us in breast cancer. And so a lot of the things that we're looking at, from a strategic standpoint, is making sure we continue our leadership position in breast cancer and then also, obviously, with the acquisition of Medivation, the same with prostate cancer. And those are 2 clear areas for us. We're really also excited. I think you talked about underappreciation for talazoparib. Because they're also

PARP inhibitors, we expect to have activity both in breast and prostate cancer, so a really great fit. And then a third real pillar of growth will be I/O, and we'll talk about, obviously, more of that today. We also, as you -- as everyone knows, just got approved 2 new hematology assets this year. And so we're excited that -- if you put those together, I've always talked about those as sort of a string of pearls. So if you think about a string of pearls for hematology, we have a nice portfolio there as well.

Seamus Christopher Fernandez - *Leerink Partners LLC, Research Division - MD, Major Pharmaceuticals and Biotechnology*

And just in terms of the dynamics with talazoparib and XTANDI, there -- what do you think -- we did see a little bit of a different trend with XTANDI, particularly after some of the data with ZYTIGA earlier this year. What's the opportunity to reverse that trend, in your view?

Elizabeth Barrett - *Pfizer Inc. - Global President, Oncology*

Well, it's hard. Because if you think about XTANDI, if you look at the underlying metastatic business while you look quarter-over-quarter from a revenue perspective, it looks -- it's actually growing quite significantly and in demand and even the metastatic setting. I don't think that the -- the new data that came out from ZYTIGA is in a completely different patient population and which is one of the reasons we're very excited about PROSPER and actually announcing the positive results of PROSPER. So the prostate cancer market is sub -- so many subpopulations with hormone-sensitive, your high-risk population, your castrate-resistant, your M0, your M1s. So it's a very complex group and subpopulation. You really have to look at those individually. So what we see with PROSPER and with EMBARK and some of the other studies that we have ongoing and ARCHES as well is we do see XTANDI working in all of those populations, and that is our expectation. So we've seen that in the PROSPER study, and obviously, those results will get communicated in the beginning of 2018. And I think once you see those results, you can sort of take a leap of what's going to happen in the continuous other studies that we're having. And so we had a very high expectation for PROSPER when we did the acquisition of Medivation.

Seamus Christopher Fernandez - *Leerink Partners LLC, Research Division - MD, Major Pharmaceuticals and Biotechnology*

Okay. And then I want to ask a little bit of an unfair question, but every once in a while, it does come up, which is we have the IMS prescriptions, but we also have some of the issues with how reimbursement has been an aid to patients. It's actually been supported. Where are we in that evolution? Just to help us think about the business and trends there.

Elizabeth Barrett - *Pfizer Inc. - Global President, Oncology*

Sure. I mean, I think as reported in our quarterly earnings, we -- we've seen that stabilize, and we expect that to stabilize. I think everyone knows that what basically happened with some questions around the ability to fund some of these foundations. It did really put a chilling effect from our ability and the industry's ability to fund. And I think some companies decided not to fund, and we've made it very public that we think that these programs are very important to patients. Patients cannot afford their medicines without them, and it's very important that these foundations exist. And we continue to support those foundations. So we believe that we'll see it stabilize. And depending on what happens, we're prepared to make sure that patients that need these medicines have these medicines.

Seamus Christopher Fernandez - *Leerink Partners LLC, Research Division - MD, Major Pharmaceuticals and Biotechnology*

Great. And why don't we talk a little bit about kidney cancer, in particular. You guys had a vote recently with SUTENT. But the kidney cancer space is evolving very, very quickly. So maybe Liz, just to start, help us understand how it's evolving, as you see, based on the data that's available today. And then maybe, Chris, you can walk us into a little bit of the Bavencio opportunity, particularly given the study with axitinib potentially reading out next year, so.

Elizabeth Barrett - *Pfizer Inc. - Global President, Oncology*

Yes. The -- to your point, the RCC business renal cell carcinoma is very crowded now. The space is evolving all the time, right? It's a very dynamic space. It's an area where there are a lot of new medicines. It's still not a curable disease, right? And the -- while we were disappointed in the vote at the ODAC, we believe very strongly in the data. And if you take a look at the data, that patients do, do better when they have SUTENT adjuvant setting. So I think we believe that it's a VEGF-driven disease, and so the combination with a VEGF is going to be important to patients in the long run. And I want to give Chris opportunity to talk about that and why that's the case. So we are looking at Inlyta as being the sort of VEGF of choice of combination. And so with that, I will turn it over to Chris and let him talk about that.

Chris Boshoff - *Pfizer Inc. - Senior Vice President and Head, Immuno-Oncology, Early Development and Translational Oncology*

Thank you. Thank you, Liz. I think to start with what Liz referred to for SUTENT, it's actually now over 10 years that SUTENT has been the standard of care for first-line metastatic renal cancer with over 250,000 patients, 0.25 million patients worldwide that's benefited from SUTENT. To Liz's point, that is a tumor that's really driven by angiogenesis because of the genetic architecture of renal cancer. So this is one of the real opportunities where we see synergism between an anti-VEGFR approach and with immunotherapy, not only because both immunotherapy and anti-VEGFR work in this disease, but because of the biology now that suggest that if you combine these 2, these 2 synergistic -- at least, biology indicates a synergism. And so we have presented previously the data with Merck with pembrolizumab and Inlyta and then also last year, the data with avelumab and Inlyta, where we reported a response rate of approximately 60%. Those were early responses in a small subset of patients. And specifically in the PD-L1 positive population, the response rate was approximately 66%. So what we're seeing with Inlyta and these combinations, the response rate looks perhaps higher than what is seen with Ipi/Nivo and response rate perhaps higher than what has been seen with atezolizumab plus -- and bevacizumab. And so we're looking forward the both studies, both Inlyta studies are recruiting well, the Phase 3 studies, and we hope to share later next year some data from these studies. Of course, the other VEGFR combinations also look encouraging, including the combination with cabozantinib and nivolumab, that's ongoing now, and pembrolizumab and lenvatinib. And I think it's great for patients with renal cancer because now we can really see a sequencing of therapies, perhaps SUTENT potentially, depending on regulatory review in the adjuvant setting, then of combination in first-line setting and then the different combinations in second or third line. So it's a real change in the paradigm in the future for this type of challenging cancer.

Seamus Christopher Fernandez - *Leerink Partners LLC, Research Division - MD, Major Pharmaceuticals and Biotechnology*

And as we think about the data that's been presented so far with the -- from Bristol, the recent presentation of data, there was, I think, some debate over the PD-L1 negative versus positive benefits. But I think we saw benefits -- lack of a benefit potentially that -- -- on PFS, but sometimes you're -- there may be some confusion on PFS and OS on a relative basis. And it seems like if you have an OS benefit and 80% of patients are PD-L1 negative, matching SUTENT on PFS is actually a pretty good result at the end of the day. So just trying to get a better sense of how you see this sort of high-risk population and intermediate-risk population evolving versus kind of the lower-risk population.

Chris Boshoff - *Pfizer Inc. - Senior Vice President and Head, Immuno-Oncology, Early Development and Translational Oncology*

That's a good -- very good question as well because we do see that in first-line metastatic renal cancer, that it may become even segmented, as you point out, between low risk, intermediate and high risk and potentially in the long term between PD-L1 positive and PD-L1 negative, where there could be a particular benefit for SUTENT in the PD-L1 negative population. I have to point out, as you know, the -- for the BMS study, PD-L1 positive and negative was really an exploratory endpoint. That was not the endpoint of the study, and so it was looking at intermediate and high risk and seeing the benefit there. And although the sub-analysis, the exploratory endpoint looked at PD-L1 positive and negative, that's probably not going to be part of the regulatory pathway for that program.

Seamus Christopher Fernandez - *Leerink Partners LLC, Research Division - MD, Major Pharmaceuticals and Biotechnology*

And so other approaches or other opportunities with Bavencio that you think Pfizer has a unique opportunity with, obviously, everybody loves to talk about lung cancer ad nauseam, how do you feel, in lung cancer, in particular, the chemo combination effort that you're doing with the JAVELIN study is progressing? And when might we see results from that?

Chris Boshoff - *Pfizer Inc. - Senior Vice President and Head, Immuno-Oncology, Early Development and Translational Oncology*

So I think I'll start, and then I want to hand over to Liz as well to talk a little bit about lung cancer because it continue -- I mean, lung cancer is, for Pfizer, an important disease. It's a disease that's becoming very segmented. Pfizer introduced Xalkori. And I think with just ceritinib and Xalkori, that really changed the paradigm for the management of lung cancer. And we have to remember, 25% to 30% of patients in the long term with lung cancer will actually be treated with targeted therapy. So in that space, apart from Xalkori, we're obviously developing lorlatinib, which is a next-generation ALK inhibitor and now in Phase 3 and in a regulatory path. And we're also developing 7775, which is a next-generation EGFR inhibitor. We recently saw the readout for dacomitinib, also second-generation EGFR inhibitor. So those are all important -- that area of oncogene-addicted lung cancer. That 25% to 30%, I think, is important for us, with Xalkori also going into the ROS1 space and potentially, in the longer term, in c-MET and that opportunity as well. We have an ongoing study that we hope to update you next year on with lorlatinib plus avelumab, so lorlatinib plus Bavencio. So that's next-generation ALK inhibitor. And the early data are encouraging, and we hope to present that next year. And then in the other cancers, the non-oncogene-addicted lung cancers, as you refer, we have referred to the 2 Bavencio studies in first line and in second-line non-small cell lung cancer, which should read out as well next year and the following year. And I think that -- and we've got many, many Phase 1 studies now, really exploring what could be the next combination with chemotherapy, with 4-1BB and OX40 with some of our other targeted for immunotherapy. So I think the long -- in the long term, lung cancer is really going to be become very, very segmented.

Elizabeth Barrett - *Pfizer Inc. - Global President, Oncology*

I think just to make a comment on your question around Bavencio, we do see, though, other areas where we will be first, think about ovarian cancer and our studies in ovarian cancer. And we're continuing to add studies and introduce studies with -- in ovarian cancer with our PARP inhibitor, talazoparib and so really excited about that space. And if you think about head and neck and the locally advanced study that we have, so we do see some areas where -- for Bavencio, where we will be first. And so while maybe not in lung cancer, the other funny thing about -- I say funny thing, it's obviously not really, it's not -- no real laughing matter, but around lung cancers, as much as it's happened in lung cancer, I was thinking the other day about high unmet need tumors, like where -- when you think about strategically where do you want to focus. And you can't help but still go to lung cancer, because despite all of the advances that we've made and the great progress we've made against lung cancer, it's still the highest unmet need cancer because the PD-1s are -- the response rate is still very low and the majority of the patients still will not benefit long term on the I/O. So we continue and especially excited about some of the combinations that we're doing in lung cancer and where -- how that might add -- have added benefit. So I think there's still a lot of area to explore in this space, in the lung cancer space, but also opportunities for us to lead outside of lung cancer.

Seamus Christopher Fernandez - *Leerink Partners LLC, Research Division - MD, Major Pharmaceuticals and Biotechnology*

And so let's talk a little bit more about the approaches outside of lung cancer, in particular. Because as I see it, we've got 3 major clinical trials that are going to potentially read out in the next 6 months, at a minimum, and those players already have market share -- more market share than Bavencio, little bit more of a leadership position. How do you sort of see the evolution of the use of Bavencio and unique combinations in some of those other areas? And maybe we can start with ovarian cancer.

Elizabeth Barrett - *Pfizer Inc. - Global President, Oncology*

Yes. So I would actually like Chris to talk about that. But before, I just want to comment about lung cancer. And we agree and understand where we are. Lung cancer is still a very large market, so it still makes sense for us to do the studies that we have in Bavencio in lung cancer. And so as Chris said, you'll see our readouts upcoming in both second-line lung cancer and first-line lung cancer. But the triplet and the doublet in lung

cancer could also be differentiating. But I think we're exactly, as I said, excited about ovarian. So Chris, why don't you talk about the studies that we have ongoing and then planned in -- for ovarian cancer?

Chris Boshoff - *Pfizer Inc. - Senior Vice President and Head, Immuno-Oncology, Early Development and Translational Oncology*

Great. Yes, thank you. So let's start with ovarian cancer and then perhaps also mention prostate cancer, because these are 2 of the tumor types that's not think of classically as hot or inflamed tumors. And so in ovarian cancer, specifically, we have 2 Phase 3 studies with chemotherapy. The first study that should readout next is the Phase -- 3 arm study should readout next year with DOXIL and with avelumab alone or DOXIL as a control arm. That's in platinum-resistant refractory ovarian cancer. And then we have the study in upfront ovarian cancer with standard of care doublet cyst platinum-based chemotherapy versus chemotherapy plus avelumab followed by avelumab and versus chemotherapy just followed by avelumab. So we -- and that study will read out the following year. So those are important studies. And then we have a number of combinations in Phase 1 in ovarian cancer as well. In prostate cancer, again, this is considered -- the vast majority of cases, at least, not the MSI high, the vast majority of cases will be considered a cold tumor. And so we have our vaccine program within that space, where we combine a prostate-specific vaccine, and it's actually called a vaccine-based immunotherapy regimen because we're combining it with PD-1, our own subcutaneous PD-1 that's developed in-house, and as well as tremelimumab. To remind you that tremelimumab, Pfizer has the rights to use -- maintain the rights to use tremelimumab within the context of a vaccine. So that program is with treme and with PD-1. And then of course, there's an ongoing Phase 3 study, an important study for us, started by Roche and sponsored by Roche, which is atezolizumab plus enzalutamide in a Phase 3-setting prostate cancer that's ongoing.

Elizabeth Barrett - *Pfizer Inc. - Global President, Oncology*

Can you talk -- Chris, just talk a little bit about avelumab and talazoparib and some of what we're looking at doing there maybe. I think that's exciting area for us as well.

Chris Boshoff - *Pfizer Inc. - Senior Vice President and Head, Immuno-Oncology, Early Development and Translational Oncology*

So I think you all know that there's a great interest in combining PARP inhibitors with checkpoint inhibitors, and perhaps some of the excitement is beyond what the clinical data has actually shown yet. And we're all aware of the recent agreements between Clovis and BMS and between AstraZeneca and Merck within this space, combining their PARP inhibitors with checkpoint. So we obviously have what we believe is a very good PARP inhibitor, talazoparib and -- plus avelumab. And we will, hopefully, in the next couple of months, announce registration in 10 studies that will start with that combination. We're starting now the Phase 1 studies as well with talazoparib plus avelumab, and we'll soon be able to announce the registration in 10 studies with that combination. The biologies or the reasons for combining is essentially threefold. First is that we now know that those tumors with DDR with DNA-repair defects, including BRCA, ATM, ATR, that in general, those are more inflamed cancers with higher PD-L1 expression. We also know that if you use a PARP inhibitor and -- on cancer cells, at least in vitro, that you upregulate proteins like STING. And as you all know, there's great interest now in STING and as a pathway. So actually, blocking PARP upregulates STING, creating that inflammatory micro environment. And I think thirdly is in the early data that was presented in prostate cancer by durvalumab plus olaparib. That was early data, but encouraging data for that combination. So that's why we're looking forward to using our medicines to start registration programs as well in this space.

Seamus Christopher Fernandez - *Leerink Partners LLC, Research Division - MD, Major Pharmaceuticals and Biotechnology*

And is there anything unique about talazoparib on some of the mechanistic aspects? So our understanding is that PARPs increase cytosolic DNA, they upregulate STING and that's one of the potential value drivers of that combination. Is there anything unique to talazoparib where you think it may, in fact, be having more of an effect?

Chris Boshoff - *Pfizer Inc. - Senior Vice President and Head, Immuno-Oncology, Early Development and Translational Oncology*

So I'll start with that and then I would refer to Liz to tell you about our EMBRACA program and where we are with that. So preclinically, I think not only data internally initially generated by BioMarin and then by Medivation and now by Pfizer as well as externally by various academic sites, and really looks like talazoparib, at least, in vitro, could be the most potent PARP inhibitor, not only from blocking PARP enzymatic activity, but talazoparib also is the most potent PARP trapper. And what it means is essentially trapping PARP on DNA, so DNA repair can't happen. And that may mean that there could be activity in combinations beyond just the classic BRCA positive tumors. So that's something we're looking at intensely in various studies, and there's additional potential activity that we can explore with talazoparib.

Elizabeth Barrett - *Pfizer Inc. - Global President, Oncology*

Yes. And I think the only thing that I'll add there is because -- as Chris mentioned, the preclinical data that suggest that talazoparib is the most potent PARP, we also get a lot of anecdotal information at this point from physicians and investigators using talazoparib that are very excited about what they're seeing and starting to see early. And we'll -- well, you'll start to see more of that get published in the coming years. But physicians that clearly see talazoparib and believe that it is the best PARP inhibitor. So we're very excited about the potential for talazoparib going forward.

Seamus Christopher Fernandez - *Leerink Partners LLC, Research Division - MD, Major Pharmaceuticals and Biotechnology*

Great. And as we kind of move towards the last couple of questions, I did want to offer the opportunity for the audience to ask questions. If you do have questions, just raise your hand. In the meantime, I will ask, of mechanisms that you're excited about, new mechanisms, whether it be novel agonists or other agents, we haven't heard much about Pfizer's efforts around IDO, so where would you kind of guide us to think about the evolving science inside Pfizer?

Elizabeth Barrett - *Pfizer Inc. - Global President, Oncology*

Yes. I'm going to let Chris talk most about it. But just want to say that there's so much out there and that -- so I think that part of our -- and we have a lot. We have 10 I/Os in the clinic today. And I think that -- my personal opinion on the IDO1 is it will be a nice addition. But what we're not seeing is the type of incremental benefit to patients that you're seeing when you're in the -- in CTLA-4. And so I think that the -- it's still to be found, I guess, is my point, right? And there's a lot to prosecute out there. There are a lot of opportunities. There's 180 different mechanisms of action in I/O today. And -- but -- and there are a couple that I'm most excited about, but being a nonscientist, I won't share those with you. But I'll turn it over to Chris and let him tell you about the ones that he's most excited about.

Chris Boshoff - *Pfizer Inc. - Senior Vice President and Head, Immuno-Oncology, Early Development and Translational Oncology*

I think just on the high level to start, that we believe that checkpoint inhibitors will be the backbone of the future of cancer medicine. And because every time you get T cells in a tumor and you get upregulation of interferon gamma, you get PD-L1 go upregulated, so you have to use an immune checkpoint inhibitor. So I always say that I believe by 2025, most patients will have immune checkpoint inhibitor as part of their cancer journey where there is adjuvant upfront, metastatic or more towards the end-stage disease. We do have -- we've now kind of consolidated and have our preclinical programs in 3 -- at 3 sites: in Pearl River in New York for the biologicals, including ADCs and nanoparticles; in La Jolla for small molecules; and in San Francisco, the Rinat site, for immunotherapies. And all of those 3 sites do -- now have the robust program for preclinically or early medicines that should enter the clinic in the next 2 years, including for immunotherapies. I want to remind you, we also do have 2 CTLA-4s that we hope to tell you more about next year, one we acquired from OncoImmune and one from BioAtla, and they should also enter the clinic within the next 2 years as well as in oncolytic virus program for cold tumors, specifically, a program that we're developing with Western Oncolytics and, again, a program that should enter the clinic in the next 24 months. I think those...

Seamus Christopher Fernandez - *Leerink Partners LLC, Research Division - MD, Major Pharmaceuticals and Biotechnology*

Yes, great. Well, with that, unfortunately, we have to wrap up. Thank you so much, Liz and Chris, for joining us, and thanks to Pfizer for coming to our meeting again this year.

Elizabeth Barrett - *Pfizer Inc. - Global President, Oncology*

Sure, absolutely. Thanks for having us. Really appreciate it. Thanks, Seamus.
