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PRESENTATION

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

Excellent. We're pleasured to have Pfizer management join us. We have Chris and Chuck joining us from Pfizer. Before we begin, maybe I'll turn over to Chuck to introduce Chris and Chuck himself, and we'll get right into it.

Charles E. Triano - *Pfizer Inc. - SVP of IR*

Yes. And great to be here. So with me is Chris Boshoff, and he is, among other things, very involved with our immuno-oncoloy division part of Pfizer. Oncology, so Chris has a vast scientific background, very fluent in clinical trials, design, all good things like that. And then for myself, I run the investor relations group at the company.

So again, thanks for having us and happy to be here. Look forward to the conversation.

QUESTIONS AND ANSWERS

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

Excellent. Well, if you don't mind, Chuck, we might start with a few sort of corporate strategy and higher-level questions with you before we dig into some of the more R&D stuff. The first one being, and this is something I've mentioned as a potential risk factor to the space, which was when you guys announced your price increases in July and then some tweets happened and you rolled it back and there was a lot of feedback shared on The Street that there may have been conversation between the President and Pfizer CEO on potentially doing something about rebates or else the increases will be back on. We're now seeing that state of California has been notified by this take in price increases in January. So my question is this, is the administration aware of that? And could we -- should we be expecting any tweets, like how should we anticipate that going into January, that the first week is already stressful as is?

Charles E. Triano - *Pfizer Inc. - SVP of IR*

Yes, back in July we announced that we were deferring our price increases, and we've continued to work with the administration, with the President, members of Congress and right, what you saw was the required notification for certain drugs. So we took that opportunity -- the California filing that we had to make, we took the opportunity mainly to be transparent on what our plans were for early 2019. So we announced some list price increases for about 10% of our portfolio. We all know that there is sometimes breathless reporting about list price increases. So we also added the points that in addition to some of those list price increases, which were modest, there would be an increase in rebates as well in that, and the net price to Pfizer, in fact, would be 0%, really no impact on net price. So for us, we wanted to be out there, be transparent. Again, our main focus is to work to ensure patients have access to medicine. And we're going to continue to work with the administration here and just if you look year-to-date

on the net price basis, we're about minus 3% globally, minus 1% in the U.S. So in the U.S., I mean, in this year, price has not been a factor for us. So we'll see. I can't predict what the administration...

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

Is that minus 1% in U.S.?

Charles E. Triano - *Pfizer Inc. - SVP of IR*

Minus 1% in the U.S., year-to-date for 2018. So we've always looked at ourselves as pricing responsibly. We are always open to discussion. That's what we're doing and really comes to ensuring access to patients. So we'll see what happens. We took that approach with being public, in the era of transparency, and so we're not trying to do anything that we hope nobody notices. And the understanding, which I think continues to grow in Washington that a price increase at the manufacturer level doesn't automatically mean that it comes straight down to our bottom line because we know there is lot of middlemen involved here.

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

And, Chuck, to be clear, when you said minus 1% in U.S. in 2018, that calculation, does that also include the genericizations that happened?

Charles E. Triano - *Pfizer Inc. - SVP of IR*

That's all -- that's only -- it doesn't necessarily include generic factors, which is another factor if you look at something like Lyrica, that would be generic mid-next year.

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

Is that included in your 2019 being...

Charles E. Triano - *Pfizer Inc. - SVP of IR*

No.

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

Okay, it's not. Okay, all right. Okay, that's important. All right, excellent. And then also M&A, since this is a question that comes up on every call, and one of the questions I get asked is, how do you define large? So Pfizer is saying we're not doing large deals. Is large $50 billion? Or is large $20 billion?

Charles E. Triano - *Pfizer Inc. - SVP of IR*

There is no real cutoff. We continue to always look at all sorts of deals and I -- maybe, if I flip it in this way, if you look at a bolt-on, right, if you look at Medivation for example, that was only really involved in terms of an integration standpoint, that only involved Pfizer, the Oncology business unit; Anacor only involved the I&I division; Hospira, bit bigger, but that was really limited to the Established Products business. So I think if you look at big, you're thinking more on an integration, disruption standpoint, something that would involve many, many parts of the company and as you probably also heard us say now, our focus really is on growth. So we always look at business development, it remains an enabler of our strategy.

It's not a strategy in and of itself, but I think, A, from the actions you've seen us in terms of investing more in R&D, investing in the pipeline, looking at capital allocation at this point with the products we have in the market, with the late-stage pipeline that we have and the confidence we have there, part of it is the choice that we've made is, well, instead of paying a premium to, say, a large company for their pipeline, we see our pipeline still is undervalued. So we're buying our own pipeline at a discount, as again as opposed to going on paying a premium to another company. So things can always change, but I think at this point, we see job one as pivoting to growth post the Lyrica LOE, making sure that we are investing and organizing for growth. We're not looking for distraction, we don't need to quote, transform ourselves. We think our internal pipeline and current products are going to transform the company and look at bolt-on. So I didn't answer the question directly. I think big -- that sort of a description of big, and right now we have made comments that, that's really not on our radar screen. Things can always change, right? And a good management team will react as the facts change, but right now are we saying, there is a big therapeutic area we're not in that we need to be in, no. Are we saying, we have no late-stage pipeline on all these LOEs. No, we have 1 big LOE left. We've got a great pipeline. So focus on more of an organic-driven growth story, accelerate that top line. We've always done a good job of leveraging the top line to the bottom line and not get involved with distractions. So that's, I think, that's our view. More apt to see tuck-ins, bolt-ons to further bolster areas that we already have and can further strengthen, but as far as Pfizer saying, we're not sure what to do, better do a big deal, that is absolutely not the case. And I'd add one thing. Generally speaking, I think, for bigger companies that have the wherewithal, big deals are -- I don't say always, but big deals are available, if the time comes, big deals generally are available, but right now we've been clear to say that's really not our focus, it's the internal story, that pivot to growth and ensuring that the whole company is focused on achieving that, and we think we have a very clear path towards that. So that's where we are now in terms of deals.

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

Excellent. And then the other one from a more high-level perspective, I do want to touch upon is, it seems like based on every press release -- incremental press release that has come out on the 2 divisions of the company, the Emerging Markets division and the Innovative side, it seems like there is an -- both sides are increasingly being run in a distinct manner and the possibility of a split looks more real or starting to look again more real, just curious what that looks like and I've gone through many iterations of a Pfizer model with 3, with 2 -- with 2 or to 1...

Charles E. Triano - *Pfizer Inc. - SVP of IR*

Yes that's right. Yes, I mean listen, job one right now, so you are right, we've organized for growth, right? So we're talking about investing for growth and organizing for growth, so yes, we have a new iteration. So the old Established Products, Essential Health business in a sense is completely being rejiggered, right? Biosimilars is coming out, going to the Innovative side, sterile injectables. So you're right, what is Established Products will be much more of an emerging markets-focused business, leadership based in China, they will have dedicated manufacturing so much more autonomous, which is what we want given the differing business models and the ability to be very quick to make decisions, being very focused. So job one is to get the new structure, particularly with the Established Products business up and running, right? Get the management in place, get everything up and running. So that's job one. So I think it'd be premature to talk about is there a split. Again, a split, if it ever made sense, I think is always available to the company, but right now job one is getting those businesses up and generating the value they can, and then we'll look at it. The market will always opine on value. The old story, at one point, it looked like there could be value and then PE multiples moved around a lot and eventually when we looked at the split, it didn't create value. So the facts changed, management took a different stance based on the facts. So the short answer is, we're always open to creating value, but right now I'd say that discussion is premature at this point. We want to first get those businesses up and running.

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

Got it. Maybe one question. One follow-up on the China business. It's currently about 7% of the top-line, probably the highest among the large pharmas. How do you expect that business to grow?

Charles E. Triano - *Pfizer Inc. - SVP of IR*

We still see the value of a branded, generic product, with Lipitor, Norvasc still the original Pfizer products continue to do very, very well. Good tailwinds in China, growing middle-class to play on quality, well not forever, is still an important play. So I think in terms of China, it's a market that continues -- I mean they have emerged, and it's a market that continues to move very quickly and one of the key drivers of us putting our management team physically in China as opposed to New York and having a 12-hour time difference is to really be part of that -- continue to be a big part of that market as it evolves very quickly, have on the ground decision-making. So a big investment for Pfizer, a big part of the world's population with increasing access to quality medicines, our ability to serve patients well, you continue to see underlying trends such as cardiovascular disease, right, in the Emerging Markets with Lipitor, Norvasc, so the portfolio, I think very focused, very in tune with what the public wants there and what the government wants. So for us that's really key drivers we saw that the incremental growth for that Established Products business more than half or about half is going to come from China in Emerging Markets, put your management team on the ground. And again, give them dedicated manufacturing, so they can make different decisions, slightly different business model. So yes, we're very -- we continue to be bullish on the China market.

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

And last one, higher-level. Consumer business, any latest there?

Charles E. Triano - *Pfizer Inc. - SVP of IR*

Nothing latest. We still expect that we will make our decision by the end of the year. We -- I know the end of the year is right around the corner so we continue to look at...

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

You got a full month?

Charles E. Triano - *Pfizer Inc. - SVP of IR*

We got a full month. So plenty working days left there, but I do expect we'll communicate one way or another hopefully what we...

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

Is an IPO being contemplated?

Charles E. Triano - *Pfizer Inc. - SVP of IR*

I'd say we're still looking at everything from IPO to keeping the business.

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

So keeping is a possibility?

Charles E. Triano - *Pfizer Inc. - SVP of IR*

Absolutely. Keeping has always been a possibility. It's a very good business, the question always has been, would it be better in someone's hands? Can we get the value we think it can potentially deliver externally, but Umer, honestly, the answer always has been...

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

So markets would determine that too. If keeping and IPO are 2 of let's say 3 possibilities, then the market conditions perhaps will also determine that.

Charles E. Triano - *Pfizer Inc. - SVP of IR*

That's right. So we're not at all opposed to keeping the business. We've been investing in the business -- it was an exercise to say, could there be value trapped here. There is no wrong answer to that. And you're right, markets have something to say about that. But yes, it's everything from status quo to full externalization to anything in between. So we're finishing up that process, and we'll communicate that possibility.

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

Excellent. Excellent. So, Chris, sorry, took a while to get to, but we just wanted to get some of high-level stuff out of the way, because people really do focus on those. I want to focus on Ibrance and the adjuvant trial in particular because I feel like over the next 12 to 18 months, this might be one of the more important readouts for a company even as large as Pfizer. First, before I begin, and, Chuck, please chime in as well, do you agree with the notion that the adjuvant indications for Ibrance could be at least as big if not bigger than the metastatic indication currently (inaudible).

Chris Boshoff - *Pfizer Inc. - Senior VP and Head of Immuno-Oncology, Translational Oncology & Early Development*

So I think that's correct. So if we look at patient numbers in the early adjuvant setting, it's probably double the number of patients than in the metastatic setting. However our studies, both PENELOPE-B and PALLAS, they're both adjuvant studies and treat stage 2 and 3 disease, so the higher-risk metastatic disease, which -- sorry, adjuvant early disease, higher-risk early disease, which represents about 50% of early disease. So the max is more of less the same number, at least the same number, early disease as metastatic disease.

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

All right. Same patient number, but isn't the duration more?

Chris Boshoff - *Pfizer Inc. - Senior VP and Head of Immuno-Oncology, Translational Oncology & Early Development*

So we recently updated the data with PALOMA-2, which is first-line metastatic with palbociclib plus letrozole versus letrozole, and the PFS reached towards palbociclib plus letrozole was over 27 months. And, of course, PFS has not directed duration of treatment, but it's a good surrogate, suggesting that there are patients that's receiving therapy beyond 24 months. In the adjuvant studies, PENELOPE-B, it's 12 months of adjuvant palbociclib and in PALLAS, it's 24 months. And PALLAS, obviously, presenting the bigger patient population, because it's the bigger cohort. It's not only the very high-risk.

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

Can you maybe spent 30 seconds with the audience on PENELOPE-B versus PALLAS trial?

Chris Boshoff - *Pfizer Inc. - Senior VP and Head of Immuno-Oncology, Translational Oncology & Early Development*

Okay. So these are 2 adjuvant setting studies. PALLAS -- both studies have completed recruitment now. PENELOPE-B, 1,250 patients; PALLAS, 5,600 patients, both completed recruitment, both studies should read out in 2020, that's our current time line. It's event-driven. These are early-disease patients with early-stage ER+, HER2- breast cancer that usually would be treated with an aromatase inhibitor, with tamoxifen with the endocrine therapy alone. So the studies are testing the hypothesis, adding palbociclib to endocrine therapy will increase invasive disease -- disease-free survival, which is the endpoint for early-stage disease. So these are the 2 biggest adjuvant studies currently running. PALLAS certainly is and should be the first CDK4, CDK6 readouts in the adjuvant setting, 2020.

Bo Chen - *Evercore ISI Institutional Equities, Research Division - Biotech & Pharma Equity Research Associate*

Okay. For the adjuvant settings, how should we think about the compliance rate? You have a Phase 2 feasibility, I would say, for the PALLAS, where it shows high 30s discontinuation rate due to AEs compared to the metastatic setting that's only teens of discontinuation rate?

Chris Boshoff - *Pfizer Inc. - Senior VP and Head of Immuno-Oncology, Translational Oncology & Early Development*

Yes, so I think from -- so just at a higher level, overall, over 150,000 woman, all patients with breast cancer have now been treated globally with palbociclib and overall, the adjuvant profile is very manageable and both patient experiences as well as physician experience has been very favorable for palbociclib and patients are motivated and patients want to do the best for themselves, for their families to have the best outcome. And so I don't necessarily believe that patients in the adjuvant setting that compliance will be less than it is necessarily in the metastatic setting. The adjuvant setting might be as good if not better than the metastatic setting. I don't know if you want to add to that?

Charles E. Triano - *Pfizer Inc. - SVP of IR*

No. I think that's fair.

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

So Chris, maybe just taking you one step forward, we saw a Phase 2 neoadjuvant study, not adjuvant, because the adjuvant, neoadjuvant trial come out. The response rate was 50% in the comparator arm, 54% in the palbo arm. So my question to you is first, how can we use that data to read across into the adjuvant setting? The response rate is not that different, but again, CDK 4/6 is not -- has much more response to it and the letrozole gets added in the adjuvant, so how do we weight in all those factors?

Chris Boshoff - *Pfizer Inc. - Senior VP and Head of Immuno-Oncology, Translational Oncology & Early Development*

So that's an important question. So you're referring to the PALLET study. The PALLET study will be presented at San Antonio Breast Cancer Conference in a couple of weeks time. This was the largest new adjuvant randomized study conducted, approximately 300 patients, randomized for 14 weeks only, so 14 weeks of treatment in the neoadjuvant setting, up-front treatment to letrozole verses letrozole plus palbociclib. And the primary endpoint in that study is a biomarker. So hypothesis-driven, it's exploratory study. It's a biomarker-driven study, with the primary endpoint or co-primary endpoint and decrease in proliferation rate as measured by specific histological test, which is called K-I 67 or Ki-67. Ki-67 or K-I 67 essentially measures tumor cell proliferation and in that endpoint we saw a significant reduction in cancer proliferation using Ki-67, with a combination palbo plus letrozole versus letrozole. Why that's important? Within the new adjuvant setting, in previous endocrine studies, including with aromatase inhibitors and with tamoxifen, Ki-67 a decrease in Ki-67 or in proliferation has been the best surrogate as a predictable outcome to -- with endocrine therapy in the adjuvant setting.

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

More so than response rate?

Chris Boshoff - *Pfizer Inc. - Senior VP and Head of Immuno-Oncology, Translational Oncology & Early Development*

Definitely more so than response rate. For 3 reasons why specifically in this study. Palbociclib, as you pointed out, even in our PALOMA-1, 2 and 3 studies, the best measure of benefit is with PFS, it's not with response rate. Number two, this is only 14 weeks of therapy. So for slow luminal ER+ breast cancer, small-proliferating cancer or low-proliferating cancer, 14-weeks treatment is a short duration. And then thirdly, response rate is measured here only by ultrasound called primary breast lesions. For lesions in the breast, the best way to actually look at decrease in size or increased size with MRI. In the study, it's only with ultrasound. And Ki-67 is certainly the most important predictor within the study of a potential benefit in the longer-term with adjuvant. Having said that, we've always said whatever the outcome of the PALLAS study, doesn't diminish our confidence in the 2 big adjuvant studies.

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

You just brought a really important point, Chris, that the response rates were measured with ultrasound not MRI in the; neoadjuvant study. In the adjuvant trial, will there be ultrasound or MRI? I actually wasn't aware of this.

Chris Boshoff - *Pfizer Inc. - Senior VP and Head of Immuno-Oncology, Translational Oncology & Early Development*

So remember in the adjuvant study, in the 2020 trial, in the big studies, the end point is not disease recurrence just in the breast. The endpoint is invasive disease-free survival. Invasive disease-free survival is measured -- it's the high dose Sloan Kettering criteria. From the time of randomization to any event and that event could be epsilateral or contralateral breast cancer, invasive breast cancer, it could be a new cancer, it could be death from any cause, it could be death from breast cancer, or it could be new metastatic disease. So the endpoint in the adjuvant study is the standard endpoint being used in adjuvant trials, invasive disease-free survival. The neoaduvant study, this is just measuring disease by ultrasound within the breast.

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

So is MRI being used then?

Chris Boshoff - *Pfizer Inc. - Senior VP and Head of Immuno-Oncology, Translational Oncology & Early Development*

So MRI is not used, but it's not that relevant because that's not the endpoint, okay?

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

Got it, got it. And so how is iDFS measured then just to be clear? So you just look for lesions anywhere?

Chris Boshoff - *Pfizer Inc. - Senior VP and Head of Immuno-Oncology, Translational Oncology & Early Development*

So invasive disease free-survival, patients are followed up and if there is any event, and that event is not there's a new lesion, it's also metastatic lesion, it's a new cancer. So obviously, death, death from any course. So any event.

Bo Chen - *Evercore ISI Institutional Equities, Research Division - Biotech & Pharma Equity Research Associate*

Got it. And what do you think is the efficacy bar as measured in DFS? Is it fair to say 85% in 5 years?

Chris Boshoff - *Pfizer Inc. - Senior VP and Head of Immuno-Oncology, Translational Oncology & Early Development*

And yes, so I don't think that's the right way of saying it. I want to come back to -- yes, so that's not 85% in 5 years. I don't think that's the -- I could come -- we can come back to that.

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

And just to be clear, in theory then, it's event-driven. So wouldn't there be an opportunity for an early interim read on these adjuvant studies?

Chris Boshoff - *Pfizer Inc. - Senior VP and Head of Immuno-Oncology, Translational Oncology & Early Development*

Are these event-driven? That's correct. Currently, we're looking at it, it's 2020. So a relatively new trial. For both studies, currently, 2020.

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

Okay. And just to be clear, is there a trial design paper published anywhere?

Chris Boshoff - *Pfizer Inc. - Senior VP and Head of Immuno-Oncology, Translational Oncology & Early Development*

A trial design paper -- on ClinicalTrials.gov is where it's published, correct, as a whole.

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

Okay. All right. That's important. Well, that's really important. That gives us a lot of work to do during the next 18 months. So Ibrance itself, there is an issue we've been looking into, which is the patent situation. So we were reasonably comfortable that the 2023 patent gets extended. We're now seeing a potential reissue process going on, which means there's a scope for invalidity. So what happened there?

Chris Boshoff - *Pfizer Inc. - Senior VP and Head of Immuno-Oncology, Translational Oncology & Early Development*

Chuck?

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

Was there a patent wear involved? External firm? So we understand what happened there.

Charles E. Triano - *Pfizer Inc. - SVP of IR*

Yes. So we'll keep our patent strategies kind of with ourselves internally. But right, we have submitted, and it's been accepted for review of patent reexamination.

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

So in your 10-K, are you going to put 2023 as the date for now?

Charles E. Triano - *Pfizer Inc. - SVP of IR*

2023 remains the date. And then this is also publicly, we have filed 2 patent term extension applications. If granted, it could be in the 2027 time frame. We remain very confident in our IP position with Ibrance.

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

You remain confident, right?

Charles E. Triano - *Pfizer Inc. - SVP of IR*

Absolutely. Absolutely.

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

And has there been incremental discussions on the recent developments internally?

Charles E. Triano - *Pfizer Inc. - SVP of IR*

No.

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

Okay. All right. And then Chris, from your perspective, we saw the PI3K alpha from Novartis come out, pretty good data. How does that impact Ibrance's duration?

Chris Boshoff - *Pfizer Inc. - Senior VP and Head of Immuno-Oncology, Translational Oncology & Early Development*

So that's a good question. So that's the -- you're referring to the SOLAR-1 study or BYL719 or alpelisib now called from Novartis, that's an important study for the field because, as you know, the PI3K inhibitors have had a very tough time, apart from the hematological disease and solid tumors for the last 10, 15 years. And a lot of companies have developed PI3K inhibitors because it's a pathway that's so active in most solid tumors. So the data from SOLAR-1 essentially is in later-stage ER+ breast cancer with fulvestrant plus alpelisib versus fulvestrant and with a significant PFS benefit. And remember, this study is only in PI3K -- PIK3CA-mutated breast cancer. So it's a biomarker selective subpopulation, which is approximately 30% of metastatic ER+ breast cancer. Some of the patients in the study did previously receive the CDK4/6 inhibitor and made tumor progress on the CDK4/6 inhibitor. I do not think that anyone thinks that alpelisib will replace a CDK4/6 in the setting of first- or second-line metastatic breast cancer, and however, I believe it's a potential good option for patients with cancers that progress on a CDK4/6 inhibitor. So it shouldn't impact directly the palbociclib patient opportunity. Having said that, we're also actually combining palbociclib with GDC-077 , the PI3K alpha-specific inhibitor from Genentech. And that's also a drug that presumably will be developed specifically in the PIK3CA-mutated tumors. And we have an internal PI3K inhibitor called gedatolisib. Gedatolisib is differentiated from the others because it's an intravenous compound given once every week. The signs with the PI3K inhibitors tells us, with PI3K, tells us that you have to really suppress very deeply the pathway, and to do that is very challenging with the continuous oral dosing. So that's why our PI3K/mTOR inhibitors, pan-PI3K, and is intravenous intermittently to really hit the target hard. And we combine currently both with letrozole, with fulvestrant plus palbociclib, and we should have some data presented in 2019 with the gedatolisib plus palbo, plus fulvestrant.

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

And do you think IV is competitive with Novartis' oral?

Chris Boshoff - *Pfizer Inc. - Senior VP and Head of Immuno-Oncology, Translational Oncology & Early Development*

And so again, the biology tells us that for these PI3K inhibitors to work, you really need to hit the target very hard. To do that with an oral compound continuously is challenging because of the side effects, including diarrhea, dermatitis and other specific side effects. And so that's why we're testing the hypothesis that it could work better to hit the target hard intermittently because you can actually achieve target coverage and still -- and manage the adverse event profile.

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

And what is the target of the alpha?

Chris Boshoff - *Pfizer Inc. - Senior VP and Head of Immuno-Oncology, Translational Oncology & Early Development*

It's a pan-PI3K inhibitor. It's also mTOR inhibitor. So it's a pan-PI3K plus mTOR. Why that's also important? In the PI3K alpha inhibitors, tumors lose a gene called PTEN, and then the pathway is activated by way of PI3K beta. So this blocks alpha, beta and delta. So it's a pan-PI3K inhibitor and an mTOR inhibitor.

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

Have we seen evidence that PI3K is not alpha-specific, have never worked in solid tumors?

Chris Boshoff - *Pfizer Inc. - Senior VP and Head of Immuno-Oncology, Translational Oncology & Early Development*

The oral compounds are challenging because you can't cover the target by giving constant -- because of the side effect profile. So that's why the differentiated intravenous approach.

Bo Chen - *Evercore ISI Institutional Equities, Research Division - Biotech & Pharma Equity Research Associate*

Got it. And how should we expect in that Phase 1 trial, the PI3K, your own in-house PI3K with palbo? Or like...

Chris Boshoff - *Pfizer Inc. - Senior VP and Head of Immuno-Oncology, Translational Oncology & Early Development*

How do we expect the effect?

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

So what measures should we expect?

Chris Boshoff - *Pfizer Inc. - Senior VP and Head of Immuno-Oncology, Translational Oncology & Early Development*

So the study is actually -- it's a study that's testing upfront, in-patients upfront with newly diagnosed metastatic disease palbociclib plus letrozole, plus gedatolisib. And then we've got an expansion cohort in tumors that are progressing on palbociclib with letrozole where the treatment is fulvestrant/palbociclib plus gedatolisib. Because it's a Phase 1b expansion, it's in a randomized study. We look at response rate, we look at complete remission and complete duration rate and duration of therapy.

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

Okay. Fantastic. Maybe turning to Xtandi, can you give us your thoughts on the metastatic hormone sensitive? How should we sort of think about handicapping that trial, what's the bar of the LATITUDE trial, et cetera, et cetera?

Chris Boshoff - *Pfizer Inc. - Senior VP and Head of Immuno-Oncology, Translational Oncology & Early Development*

Okay, very quick. So enzalutamide is approved obviously in the castrate-resistant prostate cancer, both metastatic and non-metastatic and now moving enzalutamide into earlier prostate cancer, a bit like we're moving Ibrance into adjuvant early breast cancer, moving enzalutamide into the hormone-sensitive setting of prostate cancer, which is again and obviously, a big opportunity and also providing therapy earlier, having that opportunity for patients to have a longer duration of treatment on enzalutamide compared to the metastatic setting preventing castrate-resistant disease. So we've got 2 big Phase 3 studies ongoing. Both studies completed recruitment now. The ARCHER study, that should read out in the next couple of weeks, which is in the metastatic hormone-sensitive disease setting, and EMBARK study, which should read out currently within 2020, which is non-metastatic hormone-sensitive disease. So we have 2 Phase 3 studies that should read out in this earlier setting for enzalutamide.

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

And as ZYTIGA goes generic, is there an opportunity for Xtandi to compete in that hormone-sensitive market?

Chris Boshoff - *Pfizer Inc. - Senior VP and Head of Immuno-Oncology, Translational Oncology & Early Development*

So I want Chuck to add to this as well, but remember, ZYTIGA is not a generic for Xtandi. So usually, when there's erosion, it's for a generic of a specific product. These are 2 very different compounds. Physicians do not see them actually as interchangeable. And ZYTIGA has a different safety profile. There's concomitant administration of steroids as well. It's different monitoring. So physicians see these as different compounds. So I do not believe...

Charles E. Triano - *Pfizer Inc. - SVP of IR*

No. I think that's right. I'd just emphasize the point, we don't really expect any significant degree of therapeutic substitution.

Bo Chen - *Evercore ISI Institutional Equities, Research Division - Biotech & Pharma Equity Research Associate*

Excellent. And just to clarify, ZYTIGA is approved in castration-sensitive prostate cancer, and you are targeting the hormone-sensitive prostate cancer, what's the difference there?

Chris Boshoff - *Pfizer Inc. - Senior VP and Head of Immuno-Oncology, Translational Oncology & Early Development*

So that's correct. So currently, just to start again, so enzalutamide, Xtandi, is the only small molecule that's currently approved in both metastatic and the non-metastatic setting. So it's approved in non-metastatic and metastatic castrate-resistant prostate cancer. That is where ZYTIGA is --

ZYTIGA is approved currently in the metastatic castrate-resistant prostate cancer and then in the setting of our study, ARCHERS, which is the metastatic hormone-sensitive prostate cancer.

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

Got it. So Chris, I have to ask you, on the immuno-oncoloy side, I feel like there are players in the lead. And then within the lead players, there's, like, changes happening. But where do you guys stand? How big a corporate priority is it to be a meaningful I/O player? Or is it not a corporate priority? And I know that your titles -- and it's clearly a priority for you.

Chris Boshoff - *Pfizer Inc. - Senior VP and Head of Immuno-Oncology, Translational Oncology & Early Development*

It's not about titles. It's not about titles, okay? From January, I'll be doing...

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

So you're doing away with the title, is that how we view that?

Chris Boshoff - *Pfizer Inc. - Senior VP and Head of Immuno-Oncology, Translational Oncology & Early Development*

So immuno-oncology for all of us, it's really transformative for many patients with cancer. And it will now continue to be one of the backbones for many, many cancers, not for all tumors. However, we do believe that the treatment of cancer will continue, not only to evolve with the next, what's next, what's after I/O, but also with combinations, combining small molecules with I/O, large molecules with I/O, chemotherapy, we've seen with I/O and also continue to develop new innovative therapies just combining small molecules with small molecules. So I/O will play a role that is certainly not the whole of cancer treatment, but a part of cancer treatment. We've always said that we believe combinations are the future. That's a place where we could potentially play very well because of our track record with small molecules and with the new therapies that's just been approved or recently approved for us. And so we will continue to use PD-1s and PD-L1s as backbone where it makes sense to us. As you've seen, we've recently had a positive study, a very clinically meaningful positive study with Inlyta plus avelumab. Inlyta is a small molecule for VEGFR inhibitant and first-line RCC. And that study is now being discussed globally with regulators. The other study that we worked was KEYTRUDA with Merck and done with was Inlyta plus pembrolizumab. It was also a positive read out. So Inlyta has been a very good backbone in the renal cell setting. We've got a number of studies ongoing, including Phase 3 studies with enzalutamide in prostrate cancers with PD-1s and PD-L1s. We've got a Phase 2 study -- actually, 2 Phase 2 studies with pembrolizumab and a Phase 3 study with atezolizumab with enzalutamide in castrate-resistant prostate cancer that should read out in the next 24 months. Talazoparib, we believe talazoparib is a good partner for some of the immunotherapy combination studies. The talazoparib recently approved for germline BRCA-mutated breast cancers. And TALZENNA is our new PARP inhibitor. TALZENNA is being combined with avelumab in various tumor settings in a Phase 3 study in ovarian cancer with a rational combination because we're selecting for DNA-damaged response pathway defects ovarian cancer tumors. That's a Phase 3 study. It's being combined in a tissue agnostic study, a Phase 2 study. Any tumor with a BRCA1 or BRCA2 or ATM-mutated -- mutation are being treated with talazoparib or being tested in the study, talazoparib plus avelumab. So we've got a number of strategies for immune checkpoints in combination with our in-house molecule targeted therapies.

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

So one of the theories we've been toying with is that the half-life of avelumab looks materially lower than the other PD-1s and PD-L1s. And we've been sort of working with this hypothesis that since the half-life is less than half or about half and the fact that the dosing interval actually is equivalent to the other PD-1s PD-L1s, it's being under-dosed. And that might explain some of the trials that have failed. And we then saw some recent amendments in your trials where you're now doing a potentially weekly administrations. I'm curious, how do you think about that? Is that a consideration?

Chris Boshoff - *Pfizer Inc. - Senior VP and Head of Immuno-Oncology, Translational Oncology & Early Development*

So just to go back, so the specific study which was very unfortunate that it was a negative study, it was a second-line lung cancer study and which was avelumab versus chemotherapy. And looking back at the data and a lot of analysis is obviously now being presented and, recently, at World Lung, as a conclusion, even at World Lung, it was just unlucky patients crossed over in the control arm. Over 30% of patients in the control arm went to another checkpoint, including avelumab, and compared to other studies, we are being below 20%. So that certainly have hurt the study. If we look at specific subgroups within the study where their PD-L1s high or specific disease settings, the data are comparable. It was previously published with atezolizumab or avelumab or with pembrolizumab. So I think it's difficult from that study for us to say definitely that the drug is under-dosed or that -- because there are other reasons why that study didn't succeed. The other study that was negative recently is the ovarian cancer study. So no one has tested in that setting a checkpoint inhibitor. Very difficult, very challenging disease. These are platinum-resistant, refractory ovarian cancer. For these patients, the long-term outcome is very, very poor. In fact, the control arm was DOXIL, and the response rate with DOXIL was 4%. The response rate with avelumab plus DOXIL was 14%. So it's not significantly higher, but it wasn't enough to make it a positive study. Looking back at the study, that study entered a lot of patients with very refractory disease rather than just resistant disease, where they became resistant to platinum. They never responded to platinum, refractory disease with bulky disease, and these are the patients who did particularly poorly in that study. And I think there's a lot of lessons for everyone when we present, hopefully, soon the data from that study, including the fact that there are patients that with cold tumors where it's going to be very difficult to just expect it to work by adding chemotherapy to immune checkpoints. Immunotherapy might bring T-cells in, but there's still no new epitope so the responses remained low. And then also patients with very bulky disease with poor prognosis, with low albumen, high LDH, these are patients that do not necessarily do good in any combination with an immune checkpoint.

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

Got it. Did most of JAVELIN Medley not work out the combinations in there, the 4-1BB, OX40 and all that?

Chris Boshoff - *Pfizer Inc. - Senior VP and Head of Immuno-Oncology, Translational Oncology & Early Development*

So the 4-1BB and OX40 is reading out in 2019. We should get read-outs from those. Those are the agonist studies. You've seen some data from others, from the other OX40s as well. And so those studies should read out in 2019, the combination of...

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

So they were pushed back timing-wise. I'm curious why that is.

Chris Boshoff - *Pfizer Inc. - Senior VP and Head of Immuno-Oncology, Translational Oncology & Early Development*

Actually, well, it's event-driven, the readout of the study. I think perhaps the recruitment was not as fast as we hoped in the beginning. So the readouts, getting the readouts in early 2019.

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

And is it a priority for you to take your monthly PD-1 for -- I think Chuck's one slide, there's a monthly PD-1 in development.

Chris Boshoff - *Pfizer Inc. - Senior VP and Head of Immuno-Oncology, Translational Oncology & Early Development*

So we actually have this in-house. We developed at Rinat at our San Francisco site. PD-1, it's a subcutaneous formulation. It's called [RNA88] for Rinat where it was developed. It's currently being developed as subcutaneous every 4 weeks. And we have a POC study that will read out in 2019

as well. Currently, it's very encouraging. It's particularly encouraging, the PK data, the PD data, there is no local reactions, skin reactions at the site of the injections. So it's a potentially important molecule for us in the future as well as a backbone, correct.

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

Got it. The last one, then I'll let Bo...

Bo Chen - *Evercore ISI Institutional Equities, Research Division - Biotech & Pharma Equity Research Associate*

My last question is next generation Prevnar. And so do you think that you need a large Phase 3 outcome trial like CAPiTA to get approval? Or it's okay, it's possible to just run a few maybe antibodies function measured trials to get it approved?

Charles E. Triano - *Pfizer Inc. - SVP of IR*

Yes, sure. So next generation 20 valent, right, so we've got Breakthrough Therapy Designation based on the Phase 2 data unmet need. So the short answer is, it's no. We don't expect that we'll need a large outcome study. We expect that safety profile and then noninferiority on the 20 serotype. So we use Prevnar 13 for the original 13 serotypes and then with the 23 valent, or down the market. That's how we can get the next 7. So short answer is no. We don't expect that, that will need a large outcome study. And...

Bo Chen - *Evercore ISI Institutional Equities, Research Division - Biotech & Pharma Equity Research Associate*

And do you think that Merck, your competitor, could also maybe get approval for their next-generation?

Charles E. Triano - *Pfizer Inc. - SVP of IR*

Yes. So they have a 15 valent, and I'd just give you some facts. If you look at CDC observations, so currently, Prevnar 13 being the standard. The 2 additional serotypes in the 15 valent, the competitor's 15 valent, those 2 additional serotypes are implicated for probably an incremental 10% to 15% increase in cases of invasive pneumococcal disease. If you take the next 5, so going from the 15 valent to our 20 valent, that is another 10% to 15% incremental invasive pneumococcal disease prevalence. So basically, the 20 valent is twice as effective incrementally as the 15 valent is or compared to Prevnar 13. So we think we have a very competitive market. We'll be soon starting our Phase 3 study here. I think it will be a very important competitive product in the marketplace.

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

Got it. So my last one, literally 15-second question, Chris. Your CD19 CAR-T development effort, there's now a lot of rumblings that Pfizer had it, then some of the assets were sold to Allogene. So why sell any of them? Where do we stand with the selective collaboration? Is there any data we should...

Chris Boshoff - *Pfizer Inc. - Senior VP and Head of Immuno-Oncology, Translational Oncology & Early Development*

Yes. I'm going to be very quick, and then Chuck needs to add to this one. This, we believe CAR-T cells are transformative. We wanted to place it in the hands of a place or a company where it can be very effectively, very efficiently developed, where there's a lot of the right investment to do that. So externalizing it, we still own -- we've got a 25% stake in Allogene. So it's very important for us that Allogene is successful. It's an externalization deal with 16 of our preclinical assets that will be developed by Allogene.

Charles E. Triano - *Pfizer Inc. - SVP of IR*

Yes. And I think the initial perception is actually the inverse of what we thought, right, given that the development is generally very different from a lot of the other Oncology assets, forklifted out and put it, and to Chris' point, into a company where that's all they do, right? So really, let them focus on, one, real method here, keep our equity stake here. But in terms of most efficiently allocating resources, being nimble, we thought this was the best way to actually approach this. So better outside of Pfizer, we make an interest. But this was based on our confidence in the program. And again, lack of the right term here, could it have been trapped value within Pfizer Oncology and better off somewhere else where we keep a stake, that was our decision, yes. We're thinking it can be developed very successfully in this setting.

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

Excellent. Thank you so much, Chuck. Thank you, Chris, great seeing you.

Charles E. Triano - *Pfizer Inc. - SVP of IR*

You're welcome. Thank you.
