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PRESENTATION

Jennifer Davis - *Pfizer Inc. - Director, IR*

Hi, good evening, everyone, and welcome to the Pfizer investor event at ASCO. I am Jennifer Davis, and with me today are several members of the Pfizer oncology business unit leadership team, including Mace Rothenberg, Senior Vice President of Clinical Development and Medical Affairs for the oncology BU; Glenn Andrews, Asset Franchise Leader for Torisel, Sutent and Inlyta; Bob Abraham, Senior Vice President and Chief Scientific Officer for the Oncology Research Unit; and Denise Bruns, Late Phase Development Group Leader.

So before we begin, obviously, I'd like to remind you we will make some forward-looking statements this evening during the presentation, and you can find more information about those statements in our SEC filings on Pfizer.com. With that I'll turn it over to Mace.

Mace Rothenberg - *Pfizer Inc. - SVP, Clinical Development and Medical Affairs, Oncology*

Thanks very much, Jen, and thanks to all of you who have come here and for those joining us online for spending a few minutes with us to really allow me to walk you through Pfizer oncology pipeline and what makes us excited about what we're working on at Pfizer Oncology.

So the oncology business unit has been in existence for about four years here. And the idea of creating a business unit focused on oncology was to really allow people who have focus and expertise in recognizing the challenges of oncology to focus on identifying the opportunities that existed and to be able to accelerate those drugs that look the best into development and into the market. And I think what we can say is over the past four years, we really delivered on that promise.

In 2008, 2009, we had an in-line portfolio of oncology products with three compounds; Sutent, which was launched in 2006, and then Aromasin and Camptosar, which were launched many years earlier than that.

Today, we have actually a four products in line, including Sutent and Torisel, which came over with Wyeth, but we've also have added Inlyta and Xalkori, two drugs that were developed by Pfizer internally and launched by Pfizer within the last year and are both very important drugs in their respective diseases.

I think what we now have is a diversified early portfolio that represents drugs that are targeted against elements of signaling pathways, also angiogenesis, and are all showing some signs that -- or promise in various points of development.



We also have a growing late-stage portfolio. We have two compounds that are in Phase III and I'll be able to talk about them more a little bit later. Dacomitinib in non-small cell lung cancer, and Inotuzumab for non-Hodgkin's lymphoma, and, soon, acute lymphoblastic leukemia.

In addition, we have a drug that is in regulatory review, Bosutinib for patients with CML. And then we've experienced three launches in an eight-month period between 2011 and 2012 -- Inlyta and Xalkori, as I mentioned earlier, and then Sutent received a supplemental new drug approval for pancreatic neuroendocrine tumors. So this gives you kind of what the landscape is.

But now let's look at it in terms of what I'll be focusing on today, and that is four general areas -- renal cell carcinoma, lung cancer, hematologic malignancies, and then our early development pipeline. And I think there are important messages for each of these.

For renal cell carcinoma, we are in a position of expanding our RCC leadership. We already have with Torisel and Sutent the market leadership in this disease, and now this is being expanded by the addition of Inlyta. And what this does, it provides more options for patients so that Pfizer drugs will be able to address the needs of patients at various points in their disease course.

At ASCO we are updating Inlyta second-line data in patients who had previously been treated with cytokines. And we also presented data associating rises in blood pressure with better outcomes when Inlyta is used as first-line therapy. There's also pooled Sutent efficacy data and tolerability data expanding our knowledge or insight about what this drug does and how well it's tolerated.

In lung cancer, the theme here is how we've been able to use insights into the genetics and molecular biology of lung cancer to help inform development and treatment selection. In this meeting was the first report of crizotinib, which, as you know, was approved last year for ALK-positive lung cancer patients. This has been the first presentation of the results of crizotinib in patients with a different translocation involving the ROS gene.

It was also the first report of Dacomitinib in EGFR mutant tumors in non-small cell lung cancer. So we have two very exciting drugs in that space.

Moving on to the third therapeutic area, hematologic malignancies, we have promising molecules in all stages of development. We are updating our data on Bosutinib in CML, with 30-month data from the first-line BELA trial. We will be presenting for the very first time the results of an investigator-initiated research study in relapsed acute lymphoblastic leukemia, which is very promising. And it is also the first report of crizotinib, not in non-small cell lung cancer, but actually in patients who have anaplastic large cell lymphoma. And for those of you who heard that, that was a very impressive presentation by Yael Mosse from CHOP.

And then the fourth category is our early development pipeline. We have had encouraging clinical data for multiple first-in-class compounds. I'll focus on Phase II investigator initiated research data on a CDK4/6 inhibitor in liposarcoma that will be presented by Gary Schwartz from Memorial Sloan-Kettering. And also Phase I data on a drug that targets a receptor that's associated with the TGF beta receptor family called [PF 6962], in solid tumors.

So these are the four main categories; now I'll step through each one of these.

So starting with renal cell cancer, Pfizer is the global leader in the treatment of advanced kidney cancer, and we don't throw that term around very lightly. The reason we consider ourselves a global leader is not just by market share, but by the array of products that we have, really focusing on different needs of patients in their disease course.

We had Sutent, which has been on the market in the United States since 2006, is an oral therapy, it's first-line standard-of-care for patients with advanced renal cell carcinoma, of favorable and intermediate risk. And it was the first treatment to achieve a median overall survival greater than two years. We now have six years and more than 100,000 patients have been treated with this over time.

Torisel, a drug that was acquired with the Wyeth acquisition, is an intravenous therapy, not targeting VEGF, but targeting mTOR. It's the only mTOR-approved in the first-line setting, and the only targeted agent to show an improvement in overall survival in patients with poor risk factors associated with their disease.



The newest addition to this list is Inlyta, axitinib, which is now approved in the US and Switzerland. It's also an oral therapy, and this is approved in patients who had already received prior therapy, either Sutent or cytokines, and was compared head-to-head against a target agent sorafenib, and showed significant advantages over sorafenib in the second-line treatment of RCC. So it was important in that this was the first head-to-head trial of one targeted agent versus another showing superiority of one of those two.

At this year's ASCO we are updating some of the pivotal data from the AXIS 1032 study, remember patients could have received either prior sunitinib or prior cytokines, either interferon or Interleukin-2. And this is an updated analysis of the cohort that had received prior cytokines.

What you can see here is that the median progression-free survival for those who received Inlyta was 12 months, and those who received sorafenib was 6.6 months, for a progression hazard ratio of 0.519.

This -- as I mentioned this drug was launched in February of 2012, 10 days after FDA approval, I think a testament to the ability of Pfizer to be able to position itself to produce the drug, to have it ready to be shipped and to get it in the hands of the suppliers in a very timely fashion.

Since its launch more than 1,200 prescriptions have been written. There is strong initial demand, in-line with our expectations, and there's been positive oncologist feedback. What they have told us is what they are seeing clinically in terms of the benefit of the drug, as well as side effects, is very similar to what had been reported in the pivotal trials.

Globally, as I mentioned, it was approved in Switzerland in April. We just received late last month a positive recommendation from the CHMP in the EU, which is hopefully a last step before full approval, which is expected shortly. And applications are under review in a number of other countries.

So one of the Phase II results that was presented here was, I thought, worth sharing, and this was a trial in which patients with previously untreated renal cell cancer, so this is first-line data, but in a second line setting, so it was not compared against another agent, were treated with single-agent Inlyta.

And there are some elements to the trial that are not mature yet, because the question of the trial was whether patients who were tolerating the drug well without significant side effects and without significant hypertension, how they would do if you either kept the dose stable at the starting dose or dose escalated them until they did have hypertension because of the data from Inlyta and other drugs of this class that associate increases in blood pressure with better outcomes.

Those data and those analyses are not available. What I'd like to focus your attention on is the total line that shows median progression-free survival in the first-line setting of 14.5 months and overall response rate of 48%. Again, Phase II data -- and there is a Phase III trial whose results are expected later on this year that will compare Inlyta versus sorafenib, and where we'll have more definitive information -- but I think that this gives you an idea of ballpark, of what this drug can accomplish in first-line treatment of RCC.

Now moving to lung cancer, starting with Xalkori and the value of genomic information in treatment selection for non-small cell lung cancer -- I think one of the major themes from this year's ASCO has really been the emergence of genomic characterization of tumors, not just as a research tool at major cancer centers, but actually as an important tool in the identification and referral patients for specific drugs under development, enriching the experience for patients who are most likely to benefit; and then the next logical step is incorporating that into clinical practice. I think many of us thought that was going to be five or 10 years away. I think now after this year's ASCO, we are recognizing that's going to be upon us much sooner than that.

So this -- so Xalkori launched in August, and since that time it's been prescribed by more than 800 physicians in 48 states in the United States. There has been a four-fold increase from about 10% for ALK testing when the drug was launched, to now more than 40% of physicians who are seeking ALK testing for their non-small cell lung cancer patients.

As you can see, very quickly after Xalkori was launched, the NCCN reviewed the data and incorporated ALK testing into the evaluation of patients with adenocarcinoma of the lung.



The pie chart on the right is one that you have seen before in various formats, which emphasizes the fact that when we are looking at genetic abnormalities in lung cancer, driver mutations or driver genetic abnormalities, we are not looking for that 1% or that 3% or that 5% because then the question becomes why test 100 patients if you're only going to find one or three or five. But rather the fact that if you subject those tumors to more comprehensive genetic analysis, you'll be able to find genetic abnormalities that potentially are driving the tumor in the majority of patients. 50% to 60%, in some cases, now it's up to 75%.

Now some of those abnormalities will allow you to treat the patient with a drug that's already on the market -- EGFR inhibitor for EGFR mutant patients, crizotinib for ALK-translocated patients.

But even the others that don't already have an approved product, there are drugs that are under development in testing, so therefore the referral of these patients to those clinical trials to help enrich those trials and help them understand what those drugs do in patients with those activated pathways.

So I think what we are seeing, and certainly this ASCO makes that message very loud and clear is a real paradigm shift. It's shifting right now in lung cancer, but this is not where it's going to end. It's going to continue on other cancers as we learn more about the genetic drivers of those as well.

This meeting was the first presentation of the activity of crizotinib in another molecularly characterized subset of patients, patients with ROS1 translocations.

And what I show you here is side by side waterfall charts of the registration data for crizotinib in ALK-positive non-small cell lung cancer patients, where you see approximately 88% of patients had some tumor shrinkage. And then the same kind of waterfall plot in patients with ROS1 translocations. And although there are many other fewer patients in this cohort, you see the same pattern. The vast majority of patients have had tumor shrinkage.

And, in fact, when you look at the data side by side, again, these data are not yet mature, but they are looking very similar to the ALK data at this point in this development. So as we learn more about genetic drivers of cancer, we're then able to apply those to the drugs that we have under development, refer those patients and see this kind of activity. So it's very encouraging to see this close connection between what we understand about cancer and what we can do about it.

The other drug in our lung cancer development portfolio is Dacomitinib. And as many of you know Dacomitinib targets, inhibits, not only EGFR, but other members of the HER family, HER2 and HER4. And unlike other EGFR inhibitors like Iressa and Tarceva, it is an irreversible inhibitor of these targets.

At ASCO this year for the first time, Mark Kris, from Memorial Sloan-Kettering, will be presenting the data on first-line use of Dacomitinib in a single-arm Phase II trial in patients with EGFR mutated non-small cell lung cancer.

Now we already know this is the group most sensitive to this family of compounds. So we wanted to see how well Dacomitinib did and how well it was tolerated.

And as you can see it did quite well. The objective response rate in EGFR-mutant lung cancer patients is 74%. And equally or more important is how long-lasting that progression-free survival is; it's 17 months. So this is encouraging data and we are now considering how we move this forward, but at the same time as this data is emerging we have two ongoing Phase III trials of Dacomitinib in non-small cell lung cancer.

We have the ARCHER trial 1009 that is comparing Dacomitinib head-to-head against Tarceva in patients with advanced non-small cell lung cancer. They are not selected necessarily for EGFR mutations there, but that trial was based on promising Phase II data, again, head-to-head of Dacomitinib versus Tarceva, that showed a favorable trend towards progression-free survival for Dacomitinib.

And then BR 26 is a collaboration with the NCI Canada in which patients who have already received chemotherapy and an EGFR inhibitor and have pretty much exhausted all their systemic treatment options, are then randomized to Dacomitinib versus supportive care, and that trial is accruing currently.



Now let's move to the third topic, our hematology franchise. The key here is we have multiple agents under development in various stages. I'll start with the one that's most advanced, that's Bosutinib, that is in the registration phase right now. It's under review in the US by the FDA for patients with previously treated chronic myelogenous leukemia. And it's under review at the EMA in Europe for first-line treatment of CML.

Second drug, that's still in Phase III trial is Inotuzumab Ozogamicin, and it is currently in a Phase III trial in non-Hodgkin's lymphoma and is soon to enter a Phase III trial in acute lymphoblastic leukemia.

Now let me take a moment to talk a little bit more about Inotuzumab. This is an antibody drug conjugate. So this is a very promising platform. It's targeting CD22 on militant lymphocytes, through a linker delivering the toxin calicheamicin into those cells.

There is a Phase II investigator-initiated trial that will be presented by Elias Jabbour of MD Anderson later on in this meeting that actually follows up on some very promising data presented by him last year on this drug used in this disease.

Last year, they were reporting on Inotuzumab administered once every 3 weeks, and in patients with relapsed acute lymphoblastic leukemia saw more than 50% complete remission rate, which was very encouraging.

But they also saw some signals of toxicity that concerned them, including one toxicity called veno-occlusive disease, especially in patients who had gone on to receive stem cell transplants.

That, coupled with the fact that there was some evidence that in between treatment cycles, patients' leukemias were beginning to recover, leading them to amend their study and begin to study a weekly dosing regimen where the dose was divided once every week rather than given only once every three weeks. So this meeting's presentation is going to be focused on that weekly schedule.

And what they found was, again, a very promising complete remission rate of 50%, and the median survival of more than seven months, and that was also very encouraging.

Even more encouraging is the fact that of the 10 patients who had this clinical or hematologic complete response, when they actually looked even closer for any residual clones in the peripheral blood, seven of those 10 patients were minimum residual disease negative. So PCR technology could not detect any of those malignant clones. So we are very encouraged and we're moving this to Phase III, which will open in the second half of this year.

Now stepping back, looking at our overall portfolio, I think one of the important things here is how dynamic it's been. So you see the drugs are in Phase I, Phase II and Phase III. We have very nice distribution there, but you also see drugs that have fallen out of the pipeline. And they have fallen out for different reasons. We have evaluated three compounds and felt that they did not meet our criteria to continue investing and developing those compounds, and those have been discontinued.

We have another three compounds where we felt these drugs were promising, but required expertise or amount of time or clinical development strategy that really didn't fit in with our timelines and our horizons. So it's almost like having a child that you love, and I feel that each one of these drugs has promise, but that it really could do better in someone else's household, so putting your child up for adoption. And fortunately, they have all found wonderful homes, and we feel very happy for them, Tremelimumab, Neratinib and our PARP inhibitor.

But I think what this also shows is that we have actively managed our portfolio. And over a time when I began working at Pfizer we had 32 drugs in clinical development in oncology. We now have 17. But during that time we've launched two drugs, we have two drugs in Phase III, we are accelerating one into Phase III soon, and we have actually -- even though we have reduced our R&D expenditures the overall value of our portfolio is greater now than it has ever been before. So I think it really has been with a lot of hard work by a lot of people to try and actively manage this and really focus our resources where it could make the most impact.

Talking about the most impact, you see the Kaplan-Meier curve in the lower right-hand corner. This is of a drug that some of you may not have heard of yet, but you will. And it's our CDK4/6 inhibitor. This is a drug that inhibits progression through the cell cycle from G1 to S phase. This is



the first drug in its class to reach Phase II clinical trials. The drug is now called PD 991. It doesn't have a generic name, but it should have one shortly. This is going to be presented -- not this data, but data on another disease, liposarcoma, is going to be presented by Gary Schwartz in this meeting.

And here again is another example of how we are really trying to take genomic information and really focus our development. Because in liposarcoma, the most common adult soft tissue sarcoma, 90% of these patients have over-expression activation of this pathway, over-expression of CDK4. So, therefore, if you have a CDK4 inhibitor it makes sense to evaluate that.

In that trial, the threshold was pretty low because this is a very bad disease. The threshold for success was having at least a third of the patients progression free at 12 weeks. That's how aggressive it is.

And what Gary will be presenting was actually at 12 weeks, two-thirds of the patients treated with PD 991 were progression free. So positive proof-of-concept, positive hypothesis.

The data that you are seeing on this slide is actually data that was presented a month ago at the IMPAKT breast cancer conference in Brussels. This was a follow-up to some earlier data associating CDK4 and breast cancer.

And this is a randomized Phase II trial in which patients with ER positive, HER2 negative metastatic breast cancer were randomized to letrozole alone, standard aromatase inhibitor, versus letrozole plus PD 991.

What you could see here is that the median survival for those -- median progression-free survival for those patients who received letrozole alone is 5.7 months. For those who receive letrozole plus PD 991, 18.2 months; hazard ratio for progression was 0.35.

Now, this is in 60 patients, small numbers. We have a cohort of another 90 patients that should be maturing sometime this summer. And if those results are similar to this we are going to move aggressively forward towards a larger, more definitive trial of this drug. So we are very excited about this in breast cancer and possibly in other diseases as well.

So the key takeaways for this evening, the real dynamic feature of the portfolio and incorporating a precision medicine approach that we have things going from early to late stage development; things that are in Phase III that should be reading out in the next year or two; we have a drug that's in registration; and we have two recently launched drugs.

We also have activity in four major fields - RCC, lung, hematology and early development. To that we may be adding breast cancer with PD 991 that I just mentioned, if the results hold up.

So the key takeaway for RCC - We are building our RCC portfolio and expertise to launch Inlyta and we anticipate the first-line Phase III Inlyta data in the second half of this year.

In lung cancer, the Xalkori launch and uptake has been driven by the increase in ALK testing and launches in other geographies. We have a first-in-class pan-HER inhibitor, Dacomitinib, that's currently enrolling in two Phase III trials in non-small cell lung cancer.

For hematology, Bosutinib is in regulatory reviews for CML in the US and in Europe, and we expect those decisions in the second half of this year. And we have a second Phase III trial, Inotuzumab, in ALL, to be initiated in the second half of 2012.

In early development, we have potential first-in-class position with our CDK4/6 inhibitor. And some drugs that I didn't mention because of time, our PI3 kinase mTOR inhibitors, are also showing some very promising results.

So with that I would like to stop my prepared remarks and open it up for your questions. Thank you for your attention.



QUESTIONS AND ANSWERS

Jennifer Davis - Pfizer Inc. - Director, IR

Thanks. We will also take some questions from the webcast. So here in the room, just let us know if you have got a question. We'll bring a microphone around to you.

Damien Conover - Morningstar - Analyst

Damien Conover, Morningstar. Just a question, wonder if you could talk a little bit about your strategy when you look at your earlier stage pipeline. And you've talked about moving from 32 molecules down to 17. And just wanted to get a sense of what things you are stressing in that sort of strategy. And then as you go forward, is this a strategy that will continue? And kind of the magnitude of where you see your early-stage pipeline, both in numbers and direction.

Mace Rothenberg - Pfizer Inc. - SVP, Clinical Development and Medical Affairs, Oncology

Great question. I think one of the themes that was driving us has been a move towards precision medicine. And I think that's been a critically important success factor for us.

Now I won't be arrogant to the extent of saying that every drug we develop is going to have to have a companion diagnostic biomarker to move forward, because what I realize is very often what we think we know about cancer isn't really is going on in the cancer and we could really make a terrible mistake.

But what we did is we prioritize those drugs where we do have insights into the biology, and there is some way of detecting which patients are most likely to benefit and enriching our clinical trials for that group of patients, and then being able to thoughtfully develop that.

And even in Phase I, when I started my career 25 years ago, Phase I trials were really where you looked at toxicity, tolerability and pharmacokinetics. You didn't expect to see responses. When you saw it, it was great, but not expected.

We've now shifted from where we are actually enriching these patients and we understand the drug's effect, but we do expect to see response in Phase I. And if we don't, I think that's a very ominous sign. So we've really begun to incorporate this, but we also recognize -- often we'll have to make a critical decision; when you begin to enrich the population or narrow the population, should that be right from the beginning in first-in-human studies? That's a risk because what you think you know about the disease and how it affects -- is affected by this drug may not be what you really know. But if you don't at least collect that information and then you can be able to analyze those kinds of criteria in the patients that are already on, and then determine whether or not in later stages of testing you begin to focus in on the group that's most likely to benefit. So that's one criterion, being able to understand the patients and identify those who are most likely to benefit.

The second is the development strategy. Is there a straight shot from where we are now to the next stage? What are our success criteria?

And I think one of the things that we lived through has been the PARP experience. We had the first PARP inhibitor in development. We moved that along, and then there was the BiPar PARP inhibitor presentation at ASCO about three or four years ago. And then we had fallen behind, and then we were scrambling to catch up. And then we were beginning to think, "Okay, that was triple negative breast cancer; should we go there? Or is that really the group that is the right group to develop in?"

And so, we were really at a point where we were trying to accelerate but we didn't know where to go. We didn't know which patients were most likely to benefit.

And so after a while we realized these drugs do benefit a subset of patients, but we just didn't know who they were, and it's going to require a bit more thought, a bit more association and understanding of the biology in order to really tease that out.

And for that reason we actually gave it to a company that really can focus on that and take it through those steps. And I am pretty confident that there is a benefit from this class of drugs, but it didn't meet our criteria for having a straight shot going forward.

And the third criteria is - does it really make a difference? Does it have an impact? Is it an incremental drug, or is it one that really does change a paradigm like Xalkori has done with ALK-positive lung cancers? Or the potential for a drug like PD 991 in breast cancer, or Inotuzumab in ALL?

So by shrinking our portfolio and having clear decision criteria, it really enables a wise investment of the resources we have where it's going to make the most impact and have the most value to the market and to shareholders.

Allison Yang - Barclays Capital - Analyst

Allison Yang, Barclays. Mace, if you could just comment on the launch progress of Xalkori, can you give us a sense of how many of the potential patients -- what percent of lung cancer patients are tested today? What's the availability of the FISH testing? What do you think the current share in an ALK-positive segment is? And what do you think are factors that could be deterring or impeding the growth trajectory of the product?

And finally are there -- we've heard some comments that the FISH test may be a little more time-consuming than the physician would like. Are there other developmental plans for perhaps a faster diagnostic like RT-PCR or other things in the works?

Mace Rothenberg - Pfizer Inc. - SVP, Clinical Development and Medical Affairs, Oncology

Great questions. We are fortunate to have the president of the US region, Andy Schmeltz, with us, who will be able to address some of those issues about how the launch is going in the US. Andy.

Andy Schmeltz - Pfizer Inc. - US Region President, Oncology

Thanks, Mace. I'll answer the Xalkori performance question and then give it back to you for the diagnostic future horizon.

So Xalkori is off to a good start. Obviously, the benefit risk is profound, and lung cancer treating oncologists recognize that, and we are changing behavior as the first kind of personalized medicine in lung cancer in advancing molecular testing.

Prior to Xalkori's availability less than -- about 10% of lung cancer -- non-small cell lung cancer patients were being tested for ALK, predominantly for research purposes. And we know by today there's already about 45% of non-small cell lung cancer patients being tested. So we are really excited about that because it's only over about a nine-month period that we've seen that shift.

To date, we have about 1200 new patients that have started Xalkori. And if you think about the overall incidence of ALK-positive lung cancer, say 3% to 5% of that non-small cell lung cancer population, say 5,000 to 6,000, so 1,200 is 20%, 25% in nine months on Xalkori. So that's a pretty good run rate.

Now, the reality is 45% of patients are being tested today; that means that 55% aren't yet being tested. And we are doing everything we can to advance the behavioral change that's necessary. It's not just about the oncologists, but it's also the interactions with pathologists, interventional radiologists, having sufficient tissue, and, to your point, turnaround times to get the results of the test in time to make a therapeutic decision on a patient that needs to start therapy. So everything is lined up, we are positive, and we are excited about where we can go going forward with Xalkori.

So, Mace, maybe you can comment on future diagnostic paradigms.



Mace Rothenberg - Pfizer Inc. - SVP, Clinical Development and Medical Affairs, Oncology

Thanks. So the FISH test was used in the registration studies because that is the diagnostic test that was being used to identify this in the research laboratories before we even recognize the association with Xalkori for ALK-positive patients.

And so because we had experience with that and because we had a partner in Abbott that was very willing to work with us to prepare a kit that could meet regulatory requirements for a companion diagnostic, and to do that at risk and to do that in a timeframe that matched our timeframe for bringing the drug forward, we went with the FISH test.

Clearly, it's not the only way to diagnose ALK. I see it is widely available, and we are now getting more experience and understanding what does it mean if patient is 1+, 2+ or 3+ positive. What if there is a discordance between IHC and FISH, what is truth? And also RT PCR.

Each one of those has its advantages and disadvantages. But I think what we're doing and what we think is really going to serve the best interest of patients and the community in general is to have multiple platforms, so that there are options for patients to get -- to be diagnosed, and as Andy said to be diagnosed in a timeframe that allows the initiation of treatment at a time when the patient needs that.

If we have a center that is doing the fish testing in some laboratories, but batching samples just because it's economically more attractive, and some patients are waiting three weeks for those results, that's not going to work for a patient with advanced non-small cell lung cancer. And so we have to make sure that we take away all those barriers between having a patient who should be tested and getting those test results back in a timely fashion.

Michael Yee - RBC Capital Markets - Analyst

Michael Yee, RBC. Three questions. One, you mentioned Bosutinib. Can you talk a little bit about your strategy from a competitive landscape perspective, how you're going to go about marketing that?

Second question on Xalkori, you had a slide on ROS1, which was exciting; the data that ASCO is exciting. Can you talk a little bit about how fast you can move forward there from perhaps a pivotal study, just like you did with ALK?

And then a third on Xalkori as a follow-up, in Europe, can you talk a bit about the regulatory strategy there? Do you think they need a controlled study, or they should be onboard with that the US -- a similar pathway as it was in the US?

Mace Rothenberg - Pfizer Inc. - SVP, Clinical Development and Medical Affairs, Oncology

Very good questions. So first with Bosutinib, what the strategy is -- we've actually taken two strategies. And this is really in response and working with the regulatory agencies. In the FDA they were very intrigued by the data from our study 200 that was in patients who had previously received imatinib, plus/minus dasatinib, plus/minus nilotinib. So they felt that in patients who had already received one or two or in some cases all three of these drugs that the activity, hematologic response, cytogenetic, even molecular response, was sufficient to warrant further review and submission. So they are now reviewing that.

And I think in that setting, CML is one of the poster children for molecular diagnostics and targeted therapies. But as good as it is, some patients are intolerant and some patients develop resistance. And for those patients we need alternatives, and we think that Bosutinib is potentially a good choice for those patients.

In Europe, the recommendation there was that they really wanted randomized, controlled data for the validation of this drug, so they really liked the first line trial, known as BELA. And so we filed -- we pursued that strategy there, and that's currently under review. I think when it comes to first-line treatment, each one of the available agents, imatinib, dasatinib, nilotinib and Bosutinib, have a different toxicity and tolerability profile.



There are some patients who tolerate one and not the other. There are some patients for whom one drug may not be a good choice because of underlying disease or co-morbidities. So we think having a choice of Bosutinib is very reasonable for first-line treatment of CML. So that's our approach in the two different markets.

The second question was for Xalkori and ROS1 -- we have now and I think Alice Shaw yesterday updated -- we now have 18 patients in total with ROS1 translocated non-small cell lung cancer. It's really pretty early for us to be talking about what the regulatory strategy might be.

But I think it does raise an important question, and not just for Pfizer, but for industry and for the regulatory agencies. How can one rationally develop a drug in increasingly smaller segments of a molecularly characterized disease?

And so we have interacted with them. And I think that the regulatory agencies are very interested in working with sponsors to develop ways that really make sense for the disease, for the frequency of that, and also for fulfilling the requirement for being able to diagnose these patients in a reliable fashion. So I think that is a story that will be unfolding over the next year or two.

And then Xalkori in EU, it is currently under EU review. We have been receiving and responding to questions along the way. The key there is how comfortable they are with the benefit-risk relationship. We think as we have more real-world experience with the drug, which has been consistent with the experience we've had in clinical trials, and we have additional clinical trial follow-up, that this drug is confirming a favorable benefit-risk relationship in the marketplace in the United States.

But in Europe, as you know, and in other parts of the world, there are somewhat different criteria for a regulatory approval -- different hurdles, different standards, different weighting of these elements. And, therefore, it's not at all unusual for regulatory agencies to want different information, maybe different level of maturity of information. And again the key is interacting with the regulatory agencies to make sure we are giving them what they want to be able to make their final decision.

Jennifer Davis - Pfizer Inc. - Director, IR

We have a question from the webcast. Chris Schott, JPMorgan. On Dacomitinib, he is asking for an update on the timing for the Phase III ARCHER study.

Mace Rothenberg - Pfizer Inc. - SVP, Clinical Development and Medical Affairs, Oncology

Hi, Chris. The Dacomitinib study is accruing well. It's a worldwide study. It's open at over 100 sites. We anticipate that it is going to be completing accrual in the next year or so, but, as you know, the final results of this will depend on the events. And this is driven by progression and, therefore, we have to wait for those results. So nothing imminent with that, but it's accruing well, and we are optimistic about it.

Jennifer Davis - Pfizer Inc. - Director, IR

Thanks. And he's got a follow-up, a few questions on Xalkori. How are you thinking about the competitive landscape with a couple of other ALK inhibitors in development? And how do you ensure that you maintain your position in the market? Do you have next-generation ALK inhibitors in the pipeline?

Mace Rothenberg - Pfizer Inc. - SVP, Clinical Development and Medical Affairs, Oncology

I'll give the second question to Bob Abraham, the head of our Oncology Research unit.

But the first question is, I think I counted seven compounds that are in clinical development now for ALK. I think that that's to be expected when you have kind of a paradigm-changing drug like Xalkori.



I think what we can say about Xalkori is when you have a drug where the disease control rate is about 85% to 90%, and you have a toxicity profile like that of Xalkori, that's a pretty high hurdle. And I think that there is, as we've been hearing, a very high level of satisfaction with Xalkori in the marketplace, so we feel very confident that we are delivering what the marketplace is looking for and really transformed the treatment of these patients.

And I hope that all of you have heard some of the patients self-reports of their experience with Xalkori because it really is -- it really stops you in your tracks, makes you realize why you are involved in cancer drug development.

But there are these patients who may not respond. About 15% of patients, tumors grow through crizotinib. And for those patients alternative therapies are needed. And for those portions of patients whose tumors progress after crizotinib, certainly alternatives are needed as well.

But I think that the challenge for developing a drug for crizotinib failures is that there is more than one pathway of resistance. This is not like EGFR mutant non-small cell lung cancer where more than 50% of patients who become resistant to Tarceva or Iressa do so because of T790 M mutation. Here there are at least I think 12 different either genetic abnormalities in the ALK tyrosine kinase site, or activation of an escape pathway that lead to clinical resistance.

And what Alice Shaw and Jeff Engelman from Mass General have demonstrated is that actually, one patient may have multiple mechanisms of resistance causing tumor growth.

And what makes this even more challenging is that even within a single tumor from that patient, they may be able to detect more than one resistance mechanism at work. So this makes it a really challenge for drugs to be able to address not only the one mechanism but the multiple mechanisms that might be at play.

But I think that we are only going to find out as we get more clinical data from these trials, which should be emerging over the next year or two. Bob, in terms of our follow-up for the ALK?

Bob Abraham - Pfizer Inc. - SVP and CSO, Oncology

Yes; I'd first like to reiterate Mace's comment that non-small cell lung cancer is an extremely heterogeneous disease. Therefore, there will not be one answer to the disease in patients who progressed on crizotinib. Nonetheless, we are aiming for a best-in-class molecule. We are selecting actually a candidate in a few months and we hope to be FIP, first-in-patient, in late 2013, with a backup that will address some of the perceived liabilities of crizotinib, including the resistance conferring mutations. Program is going very well. We are very optimistic that we will meet the timelines.

Mace Rothenberg - Pfizer Inc. - SVP, Clinical Development and Medical Affairs, Oncology

The other point that I think is important is the fact that although we like to consider our drugs really eloquently targeted, crizotinib targets ALK and MET and ROS. And actually we know the biological role for each of those in lung cancer and other diseases.

So as other molecules come forward that are pure ALK inhibitors and don't have some of those other characteristics, the question is, what is that going to mean in terms of clinical activity. We just don't know yet. So just something to keep in mind. Other questions?

Jennifer Davis - Pfizer Inc. - Director, IR

We've got more questions on the webcast. David Risinger, Morgan Stanley. The Xalkori is a breakthrough therapy, but its initial sales ramp has been modest. Please discuss your initiatives to boost adoption in lung cancer and your plans for development in other cancers.



Mace Rothenberg - Pfizer Inc. - SVP, Clinical Development and Medical Affairs, Oncology

That sounds like a two-part question. Andy, would you like to take the first part, and I'll take the second.

Andy Schmeltz - Pfizer Inc. - US Region President, Oncology

So David, to answer your question about adoption, so far uptake is in line with our expectations. The reality is that there is not a lot of ALK-positive lung cancer patients out there; only, as I mentioned, 5,000 to 6,000 new patients a year.

And we are changing behavior here. We are changing behavior of going from -- to enable molecular testing in lung cancer. And we knew from the beginning that it's going to take time. We are actually very bullish on the progress that we have made. And we think over time that molecular testing in lung cancer is going to be akin to HER2 testing in breast cancer. The ramp to get there in breast cancer took many years. We are going to really compress that.

As I mentioned, 45% of patients are getting tested now. We are working through with all the stakeholders that are aligned here, the turnaround time, tissue sufficiency, getting the processes in place in each of the institutions and accounts, to enable testing to become turnkey and protocols in place.

We anticipate actually that the College of American Pathology and IASLC are going to issue molecular testing in lung cancer guidelines over the next couple months, and that that's going to be an enabler for an independent committee to kind of move things forward. So we are bullish. We are not lagging. And we're doing everything we can to help connect all the stakeholders. When you talk about Xalkori and you talk about molecular testing in lung cancer, everybody nods in agreement. And it's just a little bit of time to get the processes in place, account by account, institution by institution, to enable that to be pulled through. So all systems go. It's looking good.

Mace Rothenberg - Pfizer Inc. - SVP, Clinical Development and Medical Affairs, Oncology

Very good. For the second part of your question, at this meeting Yael Mosse from the Children's Hospital of Philadelphia presented data from a pediatric trial, looking at Xalkori in patients with anaplastic large cell lymphoma. And in fact, it was in this disease that the ALK translocation was first identified in the early '90s.

And it was one of those presentations that you just had to sit back and just say, "Wow", when this report that -- of eight children with anaplastic large cell lymphoma which had relapsed in many cases, and in one case had been treated with high-dose therapy followed by stem cell transplantation, and still recurred, that eight of those eight patients went into complete remission. Eight of eight went into complete remission. That is the kind of result that you dream about.

And this is another example of us following the biology and letting biology inform the clinical trial development.

As many of you know who follow oncology drug development, the development in pediatric indications lags many years behind the development in adult indications for a variety of reasons. Here, we started almost simultaneously with getting the Phase II results with Xalkori. So I think that that's one very promising disease.

Neuroblastoma is another. And I think that that brings up another issue. The diseases that we've talked about so far were characterized by translocations that activate the ALK gene or the ROS gene. But in neuroblastoma, that's caused by a mutation or amplification of the ALK gene.

And the question becomes does Xalkori have the same clinical effect in that situation? Is the tumor driven as strongly through that one pathway as it is when there is a translocation? And she reported that indeed responses were seen, including a complete response in neuroblastoma, but not every patient responded. And so we are trying to find out, are there certain mechanisms that will determine sensitivity versus no sensitivity to Xalkori.



Now, other solid tumors, the more scientists look for ALK, the more they find it. And so now the question, and in fact we have now activated a clinical trial for -- to allow us to recruit patients with tumors other than non-small cell lung cancer, who have activation of the ALK pathway that is determined by IHC, RT PCR, or FISH, and then to allow us to get some experience with that and to be able to see if there's a signal of activity. So it's a broad Phase II trial open in multiple sites worldwide. And there is a similar companion trial going on in Europe that has slightly different eligibility criteria.

I think that only through those kinds of clinical trials will we be able to understand what other diseases, if any, are sensitive to this approach and this drug.

Jennifer Davis - Pfizer Inc. - Director, IR

Any other questions here in the room? If not, we'll take our last question then from the webcast.

Chris Schott at J.P. Morgan, one follow-up question. Are you seeing any differences in uptake in ALK testing between the US and other developed markets where you've launched?

And when we consider the ALK-positive patient as well as some of the other opportunities with Xalkori and ROS1 etc., what's the annual incidence of patients you think you can target for the drug in developed markets?

Mace Rothenberg - Pfizer Inc. - SVP, Clinical Development and Medical Affairs, Oncology

Boy, I don't know that I have the data to answer either one of those questions. So right now I think -- Denise, how many countries have approved Xalkori now?

Denise Bruns - Pfizer Inc. - VP, Late Phase Development Asset Leader, Oncology

I think it's about seven countries, Mace.

Mace Rothenberg - Pfizer Inc. - SVP, Clinical Development and Medical Affairs, Oncology

Seven countries. And so there's not a lot of experience or comparing how the uptake of molecular testing has been in some of those countries compared to the US. So I don't think we have enough information really to answer that. The second question was --?

Jennifer Davis - Pfizer Inc. - Director, IR

The patient incidence. If you look at all the different applications, ROS, other mutations for Xalkori, what you think you can target with the product.

Mace Rothenberg - Pfizer Inc. - SVP, Clinical Development and Medical Affairs, Oncology

In terms of number of patients?

Jennifer Davis - Pfizer Inc. - Director, IR

Yes, number of patients.



Mace Rothenberg - Pfizer Inc. - SVP, Clinical Development and Medical Affairs, Oncology

I guess between 5,000 and 10,000. In the US at least, I don't know; it's probably closer to 5,000 than 10,000, but it's hard to say.

The other thing is that, remember that Xalkori began its clinical evaluation in 2006 not as an ALK inhibitor because we didn't know the association between ALK and lung cancer then.

It began -- it was brought into clinical development as a MET inhibitor. And in fact, we, as many other companies, were really focused on that. And in fact we were concerned enough about the potential off-target activity against ALK that we actually were bringing forward a backup compound to Xalkori that actually had designed out the ALK-inhibitory effect. So that shows you where we were in 2006, and how we changed in 2007.

But don't forget that this is a drug that has MET inhibitory effects, and we are keeping an eye on that as we are -- and we're reporting at this meeting our Phase I experience combining Xalkori with Tarceva in Phase I.

Now the idea there is that we may have complementary drugs that cover mechanism's resistance to the other. So for Xalkori, one of the mechanisms of resistance is activation of the EGFR pathway, which Tarceva would cover.

For EGFR inhibition, one of the mechanisms of resistance is MET amplification, which Xalkori would cover. So this is kind of the rationale between developing that particular combination.

And one that's not too far behind is actually combining Xalkori with one of our own drugs, Dacomitinib, that we think is equally if not more promising.

But we have to keep in mind that MET is actually also a frequent resistant pathway in VEGF resistance. And you know how important VEGF is, and VEGF inhibitors are, in the treatment of a number of cancers. And this is just an emerging area and that we are also going to be exploring about using crizotinib in a coordinated fashion, either with or after VEGF inhibitors, to see if we can overcome that pathway of resistance.

Jennifer Davis - Pfizer Inc. - Director, IR

With that, if there are no further questions in the room, I'd like to thank Mace and team for participating and thank you all for coming tonight. Have a good rest of the conference.

Mace Rothenberg - Pfizer Inc. - SVP, Clinical Development and Medical Affairs, Oncology

Thank you very much.

Jennifer Davis - Pfizer Inc. - Director, IR

Thank you.



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