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PFE - Pfizer at Barclays Capital Global Healthcare Conference

EVENT DATE/TIME: MARCH 13, 2012 / 7:45PM GMT



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PRESENTATION

Tony Butler - *Barclays Capital - Analyst*

I'm Tony Butler, and I have the distinct pleasure to introduce Dr. Mikael Dolsten, who's Head of R&D at Pfizer. The format will be as follows. Mikael will give a few introductory comments, maybe 10 or 12 slides. We'll sit down. I've got some prepared questions. But, please, feel free to raise your hand and we'll call on you and you can throw yours up as well.

With that, Mikael?

Mikael Dolsten - *Pfizer Inc. - President, Worldwide Research and Development*

Thank you very much. So, I will share with you some of the important changes we have done in R&D to really drive biomedical innovation to deliver a pipeline of differentiated medicines that target major unmet needs for patients and payers and, overall, to ensure an R&D that can provide robust return of invested capital.

So, first of all, let me review the cautionary language. Our discussions during this presentation will include forward-looking statements. All the slides are available at our website at www.Pfizer.com.

The Pfizer R&D strategy is underpinned by three major priorities.

Delivering the portfolio in areas of focus where science and business intersect and provide feasibility and commercial attractiveness. We have executed the opportunities in our late-stage pipeline with the greatest attention over the last 15 months or so and have had six key approvals during this period. And these are the drugs that you probably have followed in the media, such as Xalkori in lung cancer, Xiapex, Eliquis for orthopedic prevention -- prevention of thromboembolism in orthopedic indications, Prevnar 13 in adults; Vyndaqel for rare disease, and Inlyta for renal cell carcinoma. So it really underlines our commitment to execute with discipline and flawless.

At the same time, I would share with you how we have renewed the pipeline with ambition to really create the sustainable R&D organization.

The second priority relates to innovating new capabilities to ensure that we increase our competitive advantage and every product we deliver is based upon unique capability for Pfizer to excel versus other active players in the field. And you can see that our priorities here includes biotech, small molecules, and vaccines capability, like a significant investment in sophisticated small molecule design, unique properties -- to target them to tissues or difficult-to-block targets. Therapeutic vaccines -- that includes our experience in conjugation technology but also novel adjuvants to raise immune response beyond what has been achieved in previous generations and antibody drug conjugates combining the selectivity of monoclonal antibodies with a power effect mechanism in chemotherapeutics.

The third priority relates to us shaping the ecosystem of the future as a key player and pioneering ways of accomplishing open external innovation such as what we have performed with our (inaudible) innovation, as well as drive precision medicine not only in oncology but across numerous diseases, whether it applies to patient selection or selection of targets with unique human genetics behind them, exemplified here by our poster child for lung cancer precision medicine, Xalkori, PCSK9, a novel target for lipid modulation, and NAV1.7, an ion channel for treatment of chronic pain conditions.



Our three strategic priorities are supplemented by three key principles on how we execute the strategy and how we accelerate it in our R&D turnaround-- the greater focus on the areas where we can compete and we see good commercial opportunities, strategic externalization to allow a more flexible and leaner cost base and differentiated innovation to pursue things in new approaches that can allow more innovation and allow Pfizer to compete at a different level.

And these three key principles drive the four levers of productivity, as I've outlined below. And let me just touch on a couple of examples related to how we have focused on improving return of investment and unlocking value for shareholders.

One of them relates to a much more rigorous portfolio of prioritization and governance culture, making sure that the technical excellence and financial metrics come together when we prioritize and have a go or no-go decision for the portfolio. And that [doesn't] include more than 90 projects that are being terminated in order to being able to focus on, really, the major drivers for innovation and financial rewards.

We have, as I've previously mentioned, put in place some very interesting open innovation models, partnered with four of the major university regions, San Francisco, San Diego, New York, and Boston, with 19 different leading academic medical centers in a new model and really focusing on novel breakthrough science in academia and supplemented then with the state-of-the-art drug design technology that has led to more than 300 proposals from academia centers, of which we currently have selected 16 for investment in and, hopefully, bringing the majority of them forward to proof of mechanism in humans.

We have implemented a significant change in where we pursue biomedical innovation and how we do it. We moved a number of our research units to the major biomedical hubs, such as Cambridge, MA or Cambridge in UK, exemplified by our pain group, cardio-metabolic group, and, soon to come, neuroscience group. And it's not only the location, but it's also how we reshape the culture, empower chief scientific officers to really take responsibility not only for the science but for the business of the science and to work with a portfolio where they are responsible from end to end for the financial performance.

Today's key, late-stage assets are described on this slide. Overall, we have 90 different programs in clinical R&D, of which 30 of them are in post proof of concept stage. And, here, I've exemplified 15 of those. In addition to what I mentioned at the onset of our six recent approvals, you can see highlighted here tofacitinib, which is in registration phase for the large rheumatoid arthritis trials that we have run. You can see Eliquis for the major indication of atrial fibrillation and stroke prevention and a drug that we have in partnership with Bristol-Myers. And, on the phase 3 post-POC programs, you can see expansion of tofacitinib into additional indications, Mening-B as a second vaccine coming behind the Prevnar 13 adult and the Dacomitinib and inotuzumab, targeted agents for different cancer indications.

I alluded to our emphasis on innovating new capabilities to improve drug design for the future. And, while we, on the left-hand side, have the most sophisticated toolbox of today, we're really focusing on increasing our capability to do even more sophisticated and more targeted agents for the future. And I've included a couple of examples here, as you can see on these slides -- tissue-distributed small molecules that show a unique distribution into organs of certain target classes, combinatorial biologics that may bind to multiple targets at the same time, or next-generation antibody drug conjugates with site-specific conjugation and ability to improve internalization of drugs into cancer cells.

Beyond the late-stage pipeline that I briefly shared with you, we have a rich early- to mid-stage clinical development pipeline. And I want just to briefly touch base on a couple of examples how we aspire to move medical practice beyond where it is today.

In immuno-inflammation, we see disease segments where, over the next five years or so, we'll see a growing population suffering from disease where current treatment is either insufficient or only provides symptomatic relief. We focus on opportunities beyond rheumatoid arthritis, as we have such an active program in registration phase with tofacitinib. And you can see some of our best-in-class or first-in-class assets -- IL6 antibody for Crohn's and lupus, MAdCAM for GI inflammatory diseases, and a p38 small molecule for COPD. And we are very excited about the opportunity to broaden the reach and improve control of inflammatory condition outside rheumatoid arthritis.

Cardiovascular continues to be the major cause of disease -- of death in diseases, and metabolic disease today affects more than 300 million patients worldwide. We see additional opportunity for innovations here, as exemplified by our PCSK9 program that just completed phase 2 trials with very encouraging data for the indication of hypercholesterolemia beyond statin treatments. We have several candidates in phase 2 for diabetes exploring



leukokinin and allowing either to improve the performance of pancreas or to act on the liver and improve glucose control. And, finally, the PDE5 inhibits an improved highly selective, once-a-day compound for diabetic nephropathy.

Within oncology, we want to really explore the power of precision medicine. There remains numerous cancer indications where there is insufficient treatment, and, in many of those indications, what we and others have celebrated success of new drugs, the treatment duration is still -- provides still room for improvement to allow long-term control of disease and cancer.

And, as you can see here, some of our clinical programs -- we have PI3K/mTOR, building on our lead in mTOR science, where we took Torisel and Rapamune as drugs to the market. And, here we have two drugs with a really best-in-class profile that now are moving forward into indications such as breast and endometrial cancer.

Our CDK4/6 inhibitor is targeted to estrogen-receptive, positive breast cancer, and we have seen encouraging properties of this compound.

And, finally, the 5T4 is an example of an antibody drug conjugate developed entirely in house, and it's the first in kind that targets cancer stem cell approach, which is, end of this year, going to enter into clinical studies. And it really shows the breadth of our precision medicine in cancer, from small molecule signal transduction inhibitor to a novel, differentiated antibody conjugate.

Vaccines is another area of significant growth in the marketplace, and we have built a platform to expand our franchise to all ages and geographies. And you can see exemplified here by targeting staphylococcus aureus, a major public health problem and multi-resistant strain. Within our therapeutic vaccine efforts, you can see a nicotine vaccine for smoking addiction and Clostridium difficile vaccine as another example of difficult-to-treat, hospitalized infections.

In neuroscience and pain, we're exploring new ways to approach brain diseases with much more emphasis on early human biology, neurofunctional imaging and patient selections using much more sophisticated methods. And, among our assets, we have a number of phosphodiesterase inhibitors targeting areas such as schizophrenia, neurodegenerative disease. We have multiple anti-amyloid approaches for Alzheimer's and also other dementia-related conditions. And, within the pain area, we have several compounds targeting novel ion channels, such as the sodium Nav family, the 1.7 and 1.8 that we are now pursuing phase 2 studies.

And, finally, in our -- the sixth area of more high-value, specialized markets -- we are increasing our presence in orphan and rare diseases such as the Factor VII to complement our hemophilia franchise and expanding the Vyndaqel drug that we have in -- just approved now in Europe for polyneuropathy. We have continued to develop the drug and seen encouraging opportunity into cardiomyopathy.

And (inaudible) biosimilar efforts, we, this year, plan to have two different, high-value antibodies into clinical studies, and the first one is Rituximab.

So let me now summarize. As you can see, we have taken important steps forward to revitalize our R&D, making really important changes, tough decisions, aiming to increase focus, more emphasis on the intersection of science and business, and building a sustainable R&D organization that can continue to deliver high-impact drugs that can provide good, robust return on investment.

Thank you for your attention.

Tony Butler - Barclays Capital - Analyst

Maybe just a couple of additional questions, if I may, before we break for the breakout session. Thank you for that introduction.

Some interesting news came out Friday from FDA regarding inotuzumab and maybe restarting those clinical trials. I'm just curious. What does that really mean with respect to NGF? Do you think you'll continue to that as you have in the past, or will that be a program you want to think about scaling in a different way.



Mikael Dolsten - Pfizer Inc. - President, Worldwide Research and Development

Yes, Tony, that's a very good question, just reflecting on yesterday's meeting for the advisory committee. So, we were encouraged to see the unanimous vote of the advisory committee, 21 to 0, that they saw a significant, unmet need in pain and that their view was support for continuous development of this anti-NGF agent in order to fully understand the benefit/risk. So we look forward to feedback and guidance from regulatory agency how this class of agents can potentially be developed. And, as you know, we have significant experience with inotuzumab in osteoarthritis.

Tony Butler - Barclays Capital - Analyst

Thank you. Just one pipeline question that you put up on the screen. PCSK9, an antibody that's very exciting, has some really good biology behind it. The question is it's development. Is it really just for familial hypercholesterolemia? Can it be used more broadly? I think Amgen also has a compound that's competing. Is there really any difference between the two molecules?

Mikael Dolsten - Pfizer Inc. - President, Worldwide Research and Development

I think what we have seen with our PCSK9 antibody is really a profound lowering of cholesterol, you know, beyond 60%. So it really takes the treatment options to a new level that hasn't been possible with small molecules before. We think that this class of drugs can be considered for patients that are either not tolerating statins or are insufficiently treated with statins. And, as we learn more about guidelines, I think the direction is that recommended cholesterol levels tend to go lower and lower, particularly for patients with multiple risk factors, like diabetics.

So we are moving into this field with the view that there is a need for broader use of an antibody like this in those patients that are not sufficiently controlled by statins. And that's, I think, far beyond the familial hypercholesterolemia class.

Tony Butler - Barclays Capital - Analyst

Okay. A question on tofacitinib. Obviously, a panel upcoming and a PDUFA date in August. I didn't hear you mention development of a once-daily. Is that still in development? And, moreover, are you thinking about other agents? I noticed you did have some compounds that were in the RA family, if you will, in your immuno-regulatory comments. But are you also thinking about other JAKs?

Mikael Dolsten - Pfizer Inc. - President, Worldwide Research and Development

We are -- I think we have built up a unique knowledge about the JAK family. And, concerning tofacitinib, as you could see from our presentation, we are developing it broadly. We have seen encouraging data in ulcerous colitis and psoriasis. We are exploring Crohn's. We have a once-daily program. And so that gives a very broad investment behind tofacitinib, which already has the first-made indication and the first in several decades of a major, novel drug class, oral, for rheumatoid arthritis patients.

We do believe that there may be a future in additional indications for different types of JAK-family drugs. So we are building on our unique knowledge about the JAK chemistry to also consider areas such as lupus, possibly multiple sclerosis. But that would be with a different JAK profile than tofacitinib. And we have some encouraging discovery data in that direction.

Tony Butler - Barclays Capital - Analyst

Thank you. Perhaps my last question, then, is around -- I've been a proponent for changes in actual R&D facilities. You've been a hero to actually create that within Pfizer to think about moving some facilities toward areas where academics tend to be very high and elevate the level of knowledge base. Can you comment about what's happening with respect to the Cambridge facility -- Cambridge, Mass. and movement, at least, of some of the Groton folks there? How far are you through that process? And I think you've actually leased some additional space, so I'd love for you to comment.

Mikael Dolsten - Pfizer Inc. - President, Worldwide Research and Development

We just returned, actually, from -- last week, I visited both Groton and Cambridge, UK. So, in Groton, we are very pleased to see that the new identity for that site, the remaining part, will really be a stronghold for more of development sciences but also some more pharmaceutical technology sciences. And that would be our internal kind of support for global capabilities, like formulations, toxicology, synthetic chemistry, and so on.

When it comes to Boston, MA, we have moved what we call biomedical innovation. We work closely with leading scientists on genetics of human disease, on reclassification of patient groups using precision medicine. And we are located on Main Street, next to the major MIT and Harvard institutions. And we were very pleased with our partnership with MIT, in which we actually are moving into one of the buildings that is on their properties.

Today, we have moved the cardiometabolic group, biology clinicians, and chemistry up to Cambridge already. And we have some 150 to 200 people in Cambridge now. And, within, actually, just a couple or three months, the neuroscience group will be located on the MIT campus.

And that will really create for us a powerhouse for biomedical innovation. And it's surrounded in a really good way. On one hand, a short commute to the Groton (inaudible) pharmaceutical R&D and then, outside, in Andover, we have our biotech group for both pharmaceutical development of antibodies and even manufacturing. So it creates, I think, a real nice corridor of innovation for us.

And that's the same how we think in California. We have a stronghold in oncology in southern California. We have a vaccine stronghold in Pearl River, New York. So we're really pleased with these changes.

And, you know, it's tough initially to make those choices, but, on the other hand, we have noticed that, once you move the organization on, you also revitalize, and you get, really, people excited about embracing change as an opportunity to move into the future and having the initiative rather than having to react to a problem.

Tony Butler - Barclays Capital - Analyst

That's excellent. Dr. Dolsten, thank you so very much for being with us today.

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