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PRESENTATION

Marc Goodman - *UBS - Analyst*

Okay, so we're going to get started with our next session. We're lucky enough to have Pfizer with us, and Mikael Dolsten, who is the President of R&D. And he has been with the Company quite a while and joined, obviously, through the Wyeth transaction.

And it is a very exciting time for Pfizer. The portfolio is really starting to come alive in R&D again. And we're looking forward to hearing a lot about it and what's next also, as well.

So, thank you for joining us. And we're going to do a breakout downstairs. Mikael is going to do a presentation for the full time up here. Okay? Thanks.

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

Thank you very much. So I'm excited to be able to share with you an update on our -- a lot of the important changes we have put in place in R&D to drive a strategy that focuses on biomedical innovation and robust return of investment for shareholders. We focus a lot on cutting-edge science and the intersection with business, and in areas where we see patients and payers displaying willingness and ability to value innovation.

First of all, I would like to share the cautionary language on this slide and that the presentation may contain forward-looking statements. These slides and the presentation is available at our website at Pfizer.com.

So, over the last couple of years we have put in place an R&D strategy that is focusing on three major priorities. Delivering the portfolio, and it's really a lot of emphasis of important science, robust technology, and an intersection where we see strong business priorities. And we have been really able to execute in this strategic change period with a strong emphasis on delivering products across the pipeline.

And as you can see here, we have had some, over the last two years, some 8 approvals we have two important drugs in filing, Eliquis and tofacitinib. And approvals include some very exciting drugs such as Xalkori for lung cancer, Inlyta for renal cell cancer, Bosulif for CML, and Prevnar 13 vaccine.

At the same time, we have sharpened some important capabilities that will set us apart from other companies when it comes to being able to design medicines and vaccines that are distinct and differentiated. And that includes the buildup of the strong industry-leading capabilities around antibody drug conjugates and novel class emerging next to the targeted small molecules in cancer therapy.

You know a lot about our strong position in the Prevnar pneumococcal vaccine franchise. Over the last couple of years we will have broadened our pipeline and capabilities into multiple -- both prophylactic, and in addition, therapeutic vaccines that really can deliver on a broad [addition] which I'm very excited about for vaccines in the future.

And we continue to push the boundaries for sophisticated small molecule design which allow us to target in novel ways, T cell selectivity or difficult-to-drug target classes such as iron channels.

Innovation, for us, goes beyond the technologies and the science, but includes a broader perspective on culture, talent, and the ecosystem of the future. And we have taken a number of initiatives to be a frontrunner when it comes to drive medical practice into much more Precision



Medicine-focused manner, where Xalkori has been the poster child for these types of approaches, and also to implement open innovation and now working with a range of academic medical centers in building up a portfolio of input from early investigators that will have complemented our internal portfolio in a fascinating and actually very additional way. And allow us, I think, to broaden the type of targets and ideas beyond what a traditional pharma has embraced.

In early 2011 we decided to accelerate our R&D strategy. I spent a lot of time with Ian Read thinking through what are the drivers for R&D productivity; what are the needs in various segments of the market for the future. And it has been, of course, very rewarding for me to work with Ian very closely in shaping the path forward for R&D, and particularly in a way taking on the challenge of how can we get a much better return of investment, unlocking value to shareholders and do it in a sustainable manner.

You can see where we have sharpened the focus on certain key areas, emphasize strategic externalization which includes select CRO partners as alliances for the future, additional biotech acquisitions and collaborations, and also building a real strong network with academia. And differentiate with innovation, emphasized by recent moves of several of our units to leading biomedical hubs, such as the Boston area and Cambridge, UK.

A lot of emphasis has been on strong execution, implementing robust decision-making; an emphasis on highly-disciplined portfolio management. And you can see here examples. We terminated some 90 projects in the pre-proof-of-concept phase. We've partnered a number of assets in later stages including our inhalation platform with Mylan.

We built up particular focus in areas where we have traditional strengths, but needed to renew, such as the new neuroscience pain unit in Cambridge. And I recently -- I mentioned our very recent move to Boston where we now have our two units, Cardiometabolic and Neuroscience, in place and fully operating. So it's really been an exciting period of redefining the strategy, emphasizing much more of where science and business intersect, and at the same time focusing on execution.

So let us look at some of the late-stage products we have here. On the left hand, key post-POC programs and on the right hand, products in registration. As you know, we are in the later phases of regulatory dialogue for Eliquis for stroke prevention in Europe and United States. And we are very encouraged by the positive dialogue, and we feel confident that we will move those forward in a positive and consistent manner here.

Tofacitinib, where we really are first in class within the JAK family of powerful immune modulating agents in rheumatoid arthritis, it was recently announced that we now have a new PDUFA date end of November. And we have submitted a number of important additional data sets to the regulatory agency. And we feel very encouraged about all the data that we have accumulated.

And we also recently announced when it comes to tofacitinib's profile, data from an additional study, 1069, that underlines how tofacitinib's influence -- in addition to signs, symptoms and patient outcome -- also structural change in a significant and important manner.

Bosulif, approved in the United States for CML, has a unique profile versus the first drug, Gleevec, to (inaudible) and also, I think, a very interesting tolerability profile that offers some advantages and distinctiveness. Xalkori, a positive opinion in Europe. And recently we submitted Viviant, or as it is written here, bazedoxifene for conjugated estrogen into Europe for registration. And that builds on our stronghold in the women's health franchise.

Now on the post-POC programs, Inlyta, we are awaiting readout later this year for a first-line study against sorafenib, or Nexavar. As you may remember, we earlier had reported second-line studies where we had a better outcome than Nexavar, so we are looking forward with excitement to that readout.

We are broadening tofacitinib into additional indications. Dacomitinib is a really interesting small molecule drug. It has an irreversible binding peptide to the EGFR receptor and covers additional members of the HER family, which makes it distinct to the traditional EGFR agents such as Tarceva, and it may also cover more resistant EGFR-expressing patient groups. We had previously reported Phase II data that showed superiority over Tarceva, and we are running a similar type of Phase III study.

Inotuzumab is one of our antibody drug conjugates. We have the drug in Phase III studies both for non-Hodgkins lymphoma in refractory patients, but also for AML. In both indications, we have seen dramatic responses really emphasizing this technology of targeting highly-potent chemotherapeutics to selective surface antigens on lymphoma or leukemia agents -- antigens.

And finally, at the end of the post-POC paragraph, you see the 991 compound or the CDK 4/6 inhibitor. We have reported at the IMPAKT cancer meeting earlier, really remarkable activity in estrogen receptor positive breast cancer, which constitute the major class of breast cancer on top of standard of care hormonal treatment where we had more than 200% improvement in PFS. And we're very excited about that remarkable activity. And we have seen additional -- similar type of responses in the second study.

Now, when it comes to building the science for the future, we looked upon Precision Medicine not only as selecting the key patient population, but really embracing that way of looking at medicine from the early starts in drug discovery.

As you can see on the left-hand, an example of selecting targets based on genetics and rare phenotypes that showed modulation of cholesterol and correlating with very favorable patient outcomes. We are now with one of the PSK9 antibodies in Phase IIb studies. In order to be really able to select the best type of dosing regimens for a best-in-class approach in this important area of going beyond statins for hypercholesterolemia treatment, the right drug or write drug combinations really is underlying on two of the examples I had -- Inotuzumab, which actually is a drug combination within one molecule; and we're also exploring expansion of Inotuzumab on different chemo backgrounds and into a different subset of lymphoma.

And finally, on selecting the right patients, and that is for us going beyond oncology. Although, of course, oncology right now is the area where you're able to much faster pick links between oncogenic drivers, diagnostics, and patient selection. But one example here that we're excited about is concerning ion channels and the Nav family where you have a number of genetically-defined pain condition, where you are able to explore your drugs earlier on, look for early signs of efficacy and then later broaden to additional larger patient populations.

So, as you can see, this is for us a different way of doing drug development and aiming to offer increased value for patients and payers.

Our technology platforms allow us to be state of the art in today's modalities. But on the right hand, you can see how we have invested to take the current modalities to a different level. And I touched briefly before on what we call tissue-specific NCEs that may allow us to target different organs, such as the liver, to deliver or different -- various demanding target classes. In the center you see examples of anti-bodies that allow you to hit two different molecules at the same time, whether you apply them as a mix or to antibodies in a hybrid molecule.

And on the lower panel you can see an example where we bring the ADC to the next generation of sophisticated agents where we have developed in-house technology that allows us to tailor exactly where on the antibody we put the payload, how we conjugate it, and application of a variety of different payloads which really will bring us beyond what we have seen in this industry before.

So, from that deliberation our late-stage pipeline, our science and technologies, I wanted to touch base for the last couple of minutes on the next wave in the pipeline. So, what's coming into Phase I and Phase II of exciting products? And of course, given data readouts, some of them will appear in the future to come on slides such as those we discussed post-POC.

Immunology and inflammation -- we saw with tofacitinib moving nicely forward into rheumatoid arthritis as the first in this JAK family, we are really taking our next priorities beyond rheumatoid arthritis, and with a vision and mission to transform inflammatory diseases into a chronic maintenance of a functionally well-performing patient. Some examples include bringing the IL6 antibodies with a really best-in-class antibody that can be giving given subcutaneously with long treatment intervals into patients with Lupus or Crohn's. The MAdCAM antibody targets specifically the receptor expressed in the gut, and allows for very selective immune suppression and is aimed for inflammation in the gastrointestinal tract, initially focused on Crohn's and ulcerative colitis.

You can see the IL-7 receptor antibody. We recently published some really exciting, unique science on the immunoregulatory function that may allow it to treat inflammatory conditions, but with far less immunosuppression than with traditional agents.



Cardiovascular metabolic disease -- we are, on one hand, highly focused on together with BMS bringing Eliquis to the market as a best-in-class anticoagulant, and at the same time looking at novel treatments that will fit our cardiometabolic experience, capability and franchise.

Glucokinase activators, it's a drug class where we have used our sophisticated small molecule capability to design a drug that has a profile that allows it to activate the glucokinase enzymes in pancreas, and allowed to boost the basal cells for sustained delivery of insulin and particularly for early phases of disease, allow for improved glycemic control and to delay onset of diabetic complications.

The power of Precision Medicine in oncology -- we were the first Company to bring mTOR agents to medical practice; Rapamune for transplantation, TORISEL for renal cell carcinoma. We have a new generation of synthetic drugs that target broader in this pathway. And we have brought into the clinic both per oral and IV agents. And we have been quite thrilled by the IV agents allowing us to get really high drug concentration and seeing encouraging responses in a number of solid tumors.

The 5T4, again an example of novel science from Pfizer. It is an antigen expressed on a subset of tumor cells. And it is those tumor cells that have the highest tumor-initiating capability, sometimes called tumor stem cells. And this unique antibody we have linked to a payload that allows us to target those cells with a very potent and effective punch. And we are planning in the next few months file IND and move into patients.

Vaccines, I alluded briefly to how excited we are in broadening our capabilities in vaccines. And we have really worked hard over the last few years to put in place the right technology. And from that comes an emerging, really renewed pipeline.

Staphylococcus aureus vaccine that is now in its second Phase II trial, to tackle a major medical problem, staph infections in environment, in hospital or care centers, and emergence of multi-resistant staph bacterium. This same type of what we call nosocomial infections includes that space would also include our efforts, or Clostridium difficile vaccine where we have developed a very novel, highly engineered vaccine to allow us to combat that emerging healthcare threat that actually leads to thousands and thousands of cases of death in hospitals after antibiotic treatment.

In the same vaccine box, you can see the nicotine vaccine. We are running our Phase I studies with a vaccine that we have designed with a lot of exploration and optimization to allow a vaccine to be designed with sophistication to induce high avidity antibodies to block effectively nicotine in the blood of smokers. And we have shown in preclinical models that we reach antibody of avidity and strength that we think go far beyond what has been studied before in this space.

You can also see that we are bringing this therapeutic vaccine to other conditions. We are in the last phase of filing an IND for clinical studies in allergic asthma and other allergic conditions driven by IGE, where we are able to raise neutralizing antibodies against IGE with additional immunoregulatory favorable properties. And we're very excited for this new wave of vaccines for different ages, different geographies and both for prophylactic and therapeutic purpose.

Neuroscience and pain has been for the industry a demanding area. The unmet need is tremendous. You have seen numbers like the economical burden in US and Europe exceeds \$1.5 trillion.

We recruited recently Michael Ehlers from Duke University. And he has worked with us to design a different type of neuroscience strategy, emphasizing a deep understanding of human biology, less importance of animal models that haven't been that predictive. And also emphasizing novel clinical study approaches that allow us to explore circuitry in psychiatry types of medicines, and also early clinical science for more neurological type of diseases.

We have several phosphodiesterase inhibitors for cognition in schizophrenia. And we also have a broad Nav family, that I mentioned before, for pain.

And finally, we see a lot of additional and complementary opportunity in high value, specialized markets such as the biosimilar drug class, that by 2020 will probably constitute several tens of billions of value in the marketplace where we can apply our long experience from top-notch pharmacy, high analytical resolution technologies and a lot of regulatory skills how to find and develop biosimilars. And we are now running Phase I-II studies on biosimilars for rituximab and trastuzumab.



Another interesting high-value market is rare diseases. There are thousands of rare diseases, and just a few percent of them have effect of treatment. And we are now in clinical studies with novel factor 7 agents with a superior profile and also approaching muscle frailty and muscular dystrophy with a novel antibody against GDFA.

I hope this has given you an insight into a very exciting portfolio from Pfizer and how we have really emphasized our turnaround of R&D on underlining return of investment, unlocking shareholder value, firm decision-making. And I look forward very much to follow up with you on questions in the breakout session. Thank you for your attention.

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