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PRESENTATION

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

Well, listen, thank you all for joining. It's a pleasure to have Pfizer's leadership team join us. We're going to go right into the R&D. But before we do, perhaps, let's turn it over to you, your highest priorities going into 2020 and things you're most looking forward to. And we'll jump right into it.

Mikael Dolsten - *Pfizer Inc. - Chief Scientific Officer and President of Worldwide Research, Development & Medical*

Yes. We were very excited about how our pipeline is projecting. Over the last number of years, we've been able to have, every year, up to 4 approvals of -- with robust drugs, and we start up to 6 pivotal studies every year. So we've been able to create a very sustainable pipeline that has close to 100 clinical projects.

Speaking particularly for now until 2020, this period, we try to summarize what you should look out for in -- that we expect to have up to 15 proof-of-concept Phase 2 data on various products that we will share externally in various forms, full conferences or top line reports. We will have 10 pivotal study starts, 5 pivotal readouts and 5 potential approvals. So we think it will be a very rich year. And the big approval ones, you could say, or readouts, maybe is -- maybe even more on your mind, is the Ibrance move into early breast cancer with the PALLAS study and Mike's area with abrocitinib for atopic dermatitis and our 20-valent adult pneumococcal conjugate vaccine. Just to give you a very brief...

QUESTIONS AND ANSWERS

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

Fantastic. Yes. No, no. That's great. Perhaps maybe the first question, I want to direct it to Chuck T., mostly because his socks are amazing today.

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

Thank you, clash with the red.

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

Chuck, there's a big question among a lot of investors that since the EPS for the company went from $3 down to -- somewhere in the $2.30 range, is there interest or a lot of appetite at Pfizer to possibly redeploy capital and bring the earnings back towards $3? Or is the company very comfortable with where the P&L stands currently and it's more focused on the internal growth drivers, not so much looking at a large external transaction right now?

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

Sure, sure. Thanks, Umer. So yes, I think we are obviously very excited about becoming a smaller science-based growth, more growthy organization, right, with certainly less dependence on, let's, for lack of a better term, call it financial engineering-type activities to drive EPS growth and more dependent and highly confident in our top line being able to deliver the EPS growth.

So as a smaller company, right, we'll have a pipeline that we would say is probably the best in our history. If you take the breadth of the products that we have in the market, patent-protected for several more years, the breadth of the pipeline that we have, right, so we're not dependent on any single currently marketed product. We're not dependent on any single pipeline product for our growth. We see a very strong top line trajectory after we do our reset with the disposition of Upjohn.

So we'll have a starting point with the new Pfizer, right? Good revenue growth. We've talked about a 6% top line CAGR really out through 2026. And then our job to your -- really, to your question, so that's going to be a nice growth period for Pfizer. The question we get is what happens when LOEs start to appear in the next 7, 8, 9 years. Now that's a long time from now, but a combination of what we've got going on internally, a lot of what we're going to talk about today and then the appetite for business development to supplement what we've got with the view that we want to have a focused number of therapeutic areas, broad opportunities within those areas and numerous opportunities.

When you look at business development for the company, we don't see a desire for a large acquisition. We don't need to transform ourselves in a sense -- what this is doing, if you look at with the disposition of Upjohn coming up, the Consumer business going out, right, Zoetis came out a few years ago, we really have transformed ourselves into a science-based, innovative, midsized big pharma company, right? So we'll reset the financials, but we're going to have very good growth off of that financial base.

So when you think about deploying capital toward business development, let me just give you a quick history just to level set everybody. A few years ago, when we were looking for end products to acquire, when we talked about revenue now as a focus of business development, you saw Hospira, you saw Medivation, you saw Anacor come in, right? So with the view today, and again backing it up with our statement that we see a nice revenue CAGR for the next many years, we've got a good quality, high-quality group of end market products. So what we're looking for to deploy capital and business development would be mid-phase products. So if you think about the question we get a lot, you have LOEs in 7, 8, 9 years, again, we know, and we're planning for that. But business development, you should expect will be, let me make 2 points: targeted more likely to products that could be launching mid next decade and products that are generally within the 5 key therapeutic areas that we're focused on and smaller deals. So...

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

Like sub-10 or sub-7?

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

Yes. So I think -- an example, again, you can never predict exactly what's going to happen. But someone asked us, would you do another Array Bioscience (sic) [Array BioPharma], right? $11 billion or so, and that brought us a nice pipeline. It did bring us some late-stage asset but a great pipeline, great people and a great platform. It's less likely that we do something like that. So if I -- let's use $10 billion. It's probably more likely that you see over the next couple of years, Pfizer is doing, again, I'll -- just to make the math easy. I'm not saying this is what the numbers will be, 20 $500 million deals rather than 1 $10 billion deal, right, so think smaller in-licensing, maybe tuck-ins. And look at what we've been doing. Array was the big one. Then we've done Vivet. We've done Therachon, so the deal with Akcea. 2 things, in our therapeutic areas and one thing that we like to say in business development, as we stick to the therapeutic areas we know and where the teams have the expertise in-house, you're less likely to make mistakes if you're analyzing molecules in an area where you have the in-house expertise. You know what to look out for. You know where the pitfalls might be, as opposed to, "Let's buy our way into a new therapeutic area where we don't have in-house expertise." You're more often to get caught up or miss things.

So mid-stage assets, think 2025 and beyond for the launch, again, you never say never if there's one-off opportunities that come in. But think more of that: smaller -- and when I say tuck-in, think much smaller, mid-phase opportunities, and we have a lot of feelers out there. Some of the recent deals that we've done, that's why I wanted to punctuate that. The most recent press releases you've seen, like, okay, yes, a few hundred million here and there in mid-stage compounds. In areas, we've done a few in gene therapy, right; oncology; internal medicine, we've done one. So the areas that we know well is where we're going to play.

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

Got it. And, Chuck, just before we move -- dig right into the R&D., should we expect any surprises on patents that are technically modeled post '25, one being Ibrance, which is in a patent reissue process technically; and the other being Eliquis, which is mostly settled but...

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

Right. Yes. No. We feel very confident. To the point on Ibrance, we get a lot of questions because today, in the Orange Book, it shows a 2023 expiry. We have already filed for the patent term extension. It has its place in line as the regulators look at that. But generally speaking, we don't look at those as something you have to go contest, right? So we are confident that the 2 extensions we filed on Ibrance, if granted, and we expect them to be granted, bring us out to at least the 2027 range.

So no, there's no sort of dangling patent issues with any of the inmarket growth drivers that we see over the next 5, 6, 7 years.

Fantastic. I think Bo has 2 hours of questions on the adjuvant trial. Bo, you want to have 5 minutes' worth?

Bo Chen - *Evercore ISI Institutional Equities, Research Division - Research Analyst*

So maybe just to level set on the Ibrance adjuvant trials, there are 2 adjuvant trials in Phase 3 ongoing. One is PALLAS with 5,600 patients in intermediate- to high-risk patients, 2-year adjuvant; and the other one is PENELOPE. That is a smaller trial, 1,500 patients -- sorry, 1,200 patients, high risk and 1-year adjuvant. So just to maybe walk through what's your rationale of running these 2 trials in parallel?

Mikael Dolsten - *Pfizer Inc. - Chief Scientific Officer and President of Worldwide Research, Development & Medical*

So we think PALLAS is the most substantial trial in the sense that it covers a broader spectrum of patients that use Ibrance for 2 years in traditional adjuvant setting, and it includes Stage 2 intermediate risk and the high-risk Stage 3 patients. And basically, it covers almost the same site in early breast cancer, as Ibrance is indicated for now in metastatic breast cancer. So it's a very large, important area for us, and it could -- for women with a risk to -- up to maybe 30% relapse in this population could offer a substantial improvement, if successful, in their life expectancy.

PENELOPE uses another approach for centers that use neoadjuvant treatment to shrink tumors, particularly in the breast but sometimes in the lymph nodes, to facilitate more minimal surgery, and it's within that group mainly focused on high risk. So it's a much more narrow population, in the PENELOPE trial, which was the first -- we started with a cooperative group. And it's a 1-year treatment of neoadjuvant, while PALLAS is 2 years.

So I would say, altogether, of course, PENELOPE add some patients, particularly those that are high risk of neoadjuvant treatment, but PALLAS is the broader trial. It's the most important, and that's a 2-year treatment paradigm. And we feel -- every trial has risk, but we feel very comfortable about the opportunity in the space given that Ibrance have shown efficacy in a number of trials, both clinical and real-world evidence trials, very consistent performance. And in this early breast cancer, we also did mechanistic studies to show that the mechanism of Ibrance to halt cell proliferation occurs to the same extent in early breast cancer cells as in the metastatic where we have run event trials.

And finally, when you move into early breast cancer, the tolerability profile and patient compliance is very important. So we did run studies like the PALLET studies and got a very favorable patient perception of using Ibrance in this setting. And we think, if you look at today, Ibrance is, by far,

the dominant market share in metastatic cancer because it's both very robust efficacy and its very compelling tolerability profile. And the latter, of course, make it even more important, minimal monitoring, less of issues with diarrhea, et cetera, that some other agents in the class have.

So from efficacy, I think there is a very strong rationale, and we are very optimistic and confident in the trial. And then from safety, we think these products have a great profile for patients. And it would -- if positive results in 2 years' use of the drug, which is about average in first-line metastatic breast cancer, and that would lead to a substantial expansion of the utility of the drug. And that's what we are hoping for. The readout is, we said, late part of 2020. As it's event trial, you can never be certain. It doesn't move into early 2021, but we think most likely late 2020. And hopefully, we can then swiftly move to filing.

Bo Chen - *Evercore ISI Institutional Equities, Research Division - Research Analyst*

Great. So maybe just to help us to size the opportunity, what are the overlap between these 2 trials? Say, what fraction of patients in PENELOPE trial would have been eligible for PALLAS and vice versa?

Mikael Dolsten - *Pfizer Inc. - Chief Scientific Officer and President of Worldwide Research, Development & Medical*

Yes. I would say it's a very -- I mean, as I said, PALLAS is the only trial that covered a large, intermediate Stage 2a and b population. While there is some overlap on the Stage 3, PALLAS is for patients that go into adjuvant treatment after surgery, radiation, et cetera, while PENELOPE is for patients that have been through a neoadjuvant treatment.

So in practical practice of oncology, the large majority of patients will be on the PALLAS indication, which is 2 years of adjuvant treatment, and we expect a much smaller number that would be eligible for PENELOPE. And that's why I said that the early breast cancer opportunity basically is equivalent in size to what you see with Ibrance in metastatic breast cancer, and the great, great majority of that would be covered by the PALLAS.

Bo Chen - *Evercore ISI Institutional Equities, Research Division - Research Analyst*

So it sounds like you expect the majority of the patients would be -- like the PALLAS patients be eligible for 2 years?

Mikael Dolsten - *Pfizer Inc. - Chief Scientific Officer and President of Worldwide Research, Development & Medical*

Absolutely, a great majority of patients.

Bo Chen - *Evercore ISI Institutional Equities, Research Division - Research Analyst*

Okay. And then you also mentioned...

Mikael Dolsten - *Pfizer Inc. - Chief Scientific Officer and President of Worldwide Research, Development & Medical*

I should say that since studies are run by cooperative group, osteo and breast cancer and colorectal cancer with the Alliance part and there's a German breast cancer group, so we haven't given detailed answer about the patient percentage as it's run by those groups, and we tend not to comment. But when I speak about the bigger picture, it's going to be dominated by the PALLAS, and the opportunity will be about the same size, the sizable size you've seen in metastatic breast cancer.

Bo Chen - *Evercore ISI Institutional Equities, Research Division - Research Analyst*

Got it. Then you also mentioned the tolerability of the drug in earlier settings, we see that there is a Phase 2 feasibility study for the PALLAS, where you see the discontinuation is in the high 30s, compared to maybe in the metastatic setting, the discontinuation is only the 10s. So with this higher discontinuation rate, how should they think about the efficacy?

Mikael Dolsten - *Pfizer Inc. - Chief Scientific Officer and President of Worldwide Research, Development & Medical*

Yes. I think as we gain more experience with Ibrance, we have been able to more effectively also inform and educate physicians that while we start on 125-milligram once daily, patients that have either low neutrophils, or for some reason, don't tolerate it well, I would say, maybe fatigue would be a typical example, that you can do dose reductions to 100 or even 75 milligram.

And what's interesting, as we have compared the patients that did have dose reduction short to dose discontinuation or delay in a cycle, it's run like 3 weeks on Ibrance then 1 week off, those patients that have reduced exposure to Ibrance still have had enough active drug to actually do about the same in outcome as the ones that have continuous treatment.

So I think you will see in the future far less patients that would discontinue the use of Ibrance as we are able to inform and educate about this. Some will do the dose reductions, but it seems to be, in studies, both clinical and additional experience we have post market, that all of the patients benefit strongly from Ibrance, even with this modification.

Bo Chen - *Evercore ISI Institutional Equities, Research Division - Research Analyst*

Could you remind us the previous data maybe in metastatic setting? What -- how do patients behave when they have the label dose versus dose reductions?

Mikael Dolsten - *Pfizer Inc. - Chief Scientific Officer and President of Worldwide Research, Development & Medical*

Yes. Since Ibrance is a drug that is very different from chemotherapeutics and you see a cell cycle arrest, particularly when combined with hormone inhibitors, have very significant impact also at the dose reduction from 125 to 100, even when you go down to 75. So the efficacy in those trials were statistically indistinguishable. They look the same, even if you did some dose reductions. So that's why I'm saying that experience is very important now for us because we can inform physicians if patients don't tolerate it well. Dose reduction will improve that rather than discontinuing the drug, and the data suggests they do about the same as the patients that stay on the higher-label dose.

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

Got it. And Mikael, just the last one on this PALLAS adjuvant topic. One of the questions that's come up has been there's been -- the cutoff for the interim analysis were intentionally kept very high because of the European regulator's requests on certain effect size on the iDFS. Can you remind us, broadly speaking, how stringent was the criteria on these interims? And has your confidence gone up based on the interims that have happened already?

Mikael Dolsten - *Pfizer Inc. - Chief Scientific Officer and President of Worldwide Research, Development & Medical*

Yes. So we tend not to give details about interim analysis and specific projects.

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

Biogen also never gave it.

Mikael Dolsten - *Pfizer Inc. - Chief Scientific Officer and President of Worldwide Research, Development & Medical*

Okay. We sometimes build in -- we're often building interim for safety and futility and sometimes for efficacy. My confidence for Ibrance was very high from the start, so I didn't need anything to move it higher. And I expect the trial to run to completion later part of 2020 and then...

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

Is that what you expected from the get-go?

Mikael Dolsten - *Pfizer Inc. - Chief Scientific Officer and President of Worldwide Research, Development & Medical*

Yes, yes, yes. We -- I think we did some amendment of PALLAS, where we increased the number of patients in order to adjust for the event rate, in general, was a little bit lower than historically. But after that change, this is what we -- we are right on time on track for a readout this year or next year or possibly early the following but I think it will happen late next year. And I expect it to run through completion. And hopefully, my strong confidence in it turns into good data set and a swift movement to a filing.

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

Right. And just before we move on, Mikael. The mechanism of action of CDK4/6s is to arrest the cell cycle, so it's cytostatic. It's not effectively killing the tumor cell. So when the event rate is low, that, to me, sounds like even the placebo arm is actually a little more cytostatic than we would have expected. Does that raise the risk in the trial?

Mikael Dolsten - *Pfizer Inc. - Chief Scientific Officer and President of Worldwide Research, Development & Medical*

No. I think you see often studies that run over many years that when you predict event rates, historically versus today, there may be some minor improvement in general care of patients in how they are often diagnosed, maybe slightly earlier than in the past. So it wasn't any big surprise for us. We see that happening in many trials. And the mechanism has proven in the first-line and second-line patients to be very effective, very consistent. We reported real-world evidence data from patients in medical practice and therefore perform greatly on Ibrance, whether you look at progression-free survival. And also, we start to generate overall survival in medical practice, very encouraging positive data. So we think the mechanism is very robustly proven, and I see no scientific rationale why it wouldn't be as effective in early breast cancer based on all the scientific studies we have done clinical and preclinically.

I should say that we have been pioneers in this space, our own CDK4/6, and we actually have a follow-on drug for patients that are resistant, whether intrinsically or acquired a CDK2/4/6 that's now running a Phase 1b study could be a great opportunity. And we've also developed as part of our thinking of life cycle management a CDK4 single compound and a CDK2 single compound to cover the needs of a variety of different patients in breast -- in different aspects of breast cancer but also going far beyond breast cancer. And the 2 others, we plan to have in clinical studies next year. The CDK2/4/6 may already next year have some early clinical data coming. So it's an expansion of the franchise based on our confidence in its importance for breast and for other tumors.

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

Got it. So we'll also have 2 hours of questions on the pneumococcal vaccine. But before we get there, perhaps, let's spend some time on the JAK franchise for a minute.

Mike, before we dig into -- and we're going to -- I'm going to try to do this quick because we have 19 minutes remaining. Before we dig into abrocitinib, I guess one question I've had has been it seems like FDA is giving a black box to the class now, and they effectively said that in upadacitinib

review. However, the launch curve for the AbbVie JAK has looked different than it did for the Lilly JAK. So, a, what's your expectation that the class label will continue beyond? And how does that impact or not impact how you're thinking about resource allocation to various JAK programs?

Michael S. Vincent - *Pfizer Inc. - Senior VP and Chief Scientific Officer of Inflammation & Immunology Research & Development*

Well, I think the recent events would suggest that at least for JAK1 selective inhibitors, the labeling approach may likely be quite similar across the class. I think what...

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

Using a JAK1 selective not JAK?

Michael S. Vincent - *Pfizer Inc. - Senior VP and Chief Scientific Officer of Inflammation & Immunology Research & Development*

Well, I think that all the molecules out there now that have those black box warnings also have JAK1 coverage. I think what's becoming clear as we look at more selective inhibitors is that we see a different biochemical profile. The molecules behave differently in the clinic in patients. We see that both on the efficacy side. We see it with clinical laboratories. You only know about rare side effects by studying large numbers of patients for long periods of time. So by definition, for the more selective agents now that we know behave differently, what the ultimate safety profile is going to look like is something we're going to have to wait for the data. And I can't -- unfortunately, I can't -- I don't have a crystal ball as to how the FDA approaches future safety data sets. But I think what it appears right now is a JAK1 selective inhibitor is likely to be approved with a black box.

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

Do you expect to hit superiority over dupi in the upcoming Phase 3 trial? I think it's due this year, right?

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

Early next year.

Michael S. Vincent - *Pfizer Inc. - Senior VP and Chief Scientific Officer of Inflammation & Immunology Research & Development*

Early next year. So the -- one of our Phase 3 studies has a comparative arm that both compares to abrocitinib at 200 milligrams and 100 milligrams placebo. As a key secondary endpoint, there's a comparison to dupilumab on a number of endpoints.

I think what we've seen -- you can never be sure about cross-comparisons, but what we've seen very consistently in our Phase 2 data sets that we presented publicly as well as our first Phase 3 data set and our most recent Phase 3 data set, which is a placebo-controlled trial, the results have been remarkably consistent. Really, no decrement between Phase 2 and Phase 3. The safety profile has been very consistent. And the other thing that has -- that we think it seems quite likely is that the impact on itch is much more rapid with abrocitinib than with dupilumab. Mechanistically, we think that relates to the fact that JAK1 inhibition covers IL-31, and IL-31 is a direct stimulant of itching in the nerve cells. So we think that's why, mechanistically, there's a more rapid response. So we've seen a response that we can measure statistically in Phase 2 as early as 2 days.

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

Does itch drive the IgA endpoint?

Michael S. Vincent - *Pfizer Inc. - Senior VP and Chief Scientific Officer of Inflammation & Immunology Research & Development*

It's a separate endpoint from IgA. But from a patient-centric standpoint, it's probably the thing that drives patients most crazy and that they're most interested in seeing relieved rapidly and effectively. So we think that will be a differentiator in the marketplace in addition to being an easy-to-use oral alternative that has high efficacy.

Mikael Dolsten - *Pfizer Inc. - Chief Scientific Officer and President of Worldwide Research, Development & Medical*

So Mike, when you said that you were impressed with the days 2 -- a week or 2 relief for itch with abrocitinib, what was the historical time for dupi to have efficacy?

Michael S. Vincent - *Pfizer Inc. - Senior VP and Chief Scientific Officer of Inflammation & Immunology Research & Development*

It's really out to the 12-, 16-week time point that where you see the point separate. And that -- it kind of makes sense because you're hitting upstream cytokine mechanisms. And downstream of that, you get the itch relief.

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

Right.

Mikael Dolsten - *Pfizer Inc. - Chief Scientific Officer and President of Worldwide Research, Development & Medical*

We are not talking just about hours a day. We're talking about...

Michael S. Vincent - *Pfizer Inc. - Senior VP and Chief Scientific Officer of Inflammation & Immunology Research & Development*

Weeks.

Mikael Dolsten - *Pfizer Inc. - Chief Scientific Officer and President of Worldwide Research, Development & Medical*

Many weeks' difference in -- that's terrific.

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

Got it. Got it. And, Mike, also, can you remind us how many DVTs have happened in abrocitinib development to date?

Michael S. Vincent - *Pfizer Inc. - Senior VP and Chief Scientific Officer of Inflammation & Immunology Research & Development*

I don't think we've reported any in the study so far.

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

And for that reason, do we expect the label to look potentially different?

Michael S. Vincent - *Pfizer Inc. - Senior VP and Chief Scientific Officer of Inflammation & Immunology Research & Development*

Our expectation has been that we will have a black box warning, and that's based on what we've seen from the FDA recently. We think that's a reasonable expectation.

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

Is there any platelet impact?

Michael S. Vincent - *Pfizer Inc. - Senior VP and Chief Scientific Officer of Inflammation & Immunology Research & Development*

We do see -- and this is a pharmacodynamic effect of many JAK inhibitors. We do see a measurable decrease in platelets but not a clinically significant decrease. So we're not seeing patients who need to come off drug for thrombocytopenia. We're not seeing bleeding events, petechiae, things that indicate a functional platelet problem.

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

Got it. And then before we move on from the JAK topic, I did want to also ask. Some of the data you guys put up for alopecia was truly remarkable. And the question I've had is how should we think about -- and this may not necessarily be an R&D question per se, but how should we think about -- is that an aesthetic-like pricing? Or is that a medical -- like how does -- you talk to payers and you show some of the clinical profile you've generated. Does this seem more like a medical indication or an aesthetic indication?

Michael S. Vincent - *Pfizer Inc. - Senior VP and Chief Scientific Officer of Inflammation & Immunology Research & Development*

Well I'm not the right person to talk about pricing, but I have talked to a lot of patients, and this is a devastating disease from a psychosocial standpoint, in particular, I think, adolescents, young adults who are impacted by this disease. It's -- the psychosocial impact is clear. We were able to measure it with patient-reported outcomes, even in our relatively small Phase 2 study. And you only need to go to YouTube and listen to some patients talk about this disease to understand that this is not strictly a cosmetic disease.

First of all, it's the immune system that's misbehaving and eliminating hair cells. It can become permanent. It can affect all areas of the body. I don't think there's any question that this is a severe medical condition.

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

Got it. Okay. And then just very briefly, a lot of SMID biotechs have looked into doing topical JAKs to follow the lead of a lot of what Pfizer has done. I remember you guys had something in topical and it's no longer there. Is that still of interest?

Michael S. Vincent - *Pfizer Inc. - Senior VP and Chief Scientific Officer of Inflammation & Immunology Research & Development*

Absolutely. We -- dermatologists like to use topical therapies. Some patients have much more mild disease, and a systemic therapy doesn't have the right risk-benefit profile for them. We have 2 ongoing Phase 2b studies with a topical TYK2/JAK1 inhibitor, which we think will treat both atopic dermatitis and psoriasis. We've seen the ORR data from the TYK2/JAK1 looks really outstanding in psoriasis that we anticipate we'll get good results from both of those molecules, one administered topically.

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

Got it. So in 13 minutes, let's do pneumococcal, C. diff, gene therapy, Array and many more.

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

Well, fire on, yes and no answers.

Bo Chen - *Evercore ISI Institutional Equities, Research Division - Research Analyst*

So let's then talk about pneumococcal conjugate vaccines. First, I want to confirm whether for the adult indication for PCV20, do you need 2 Phase 3s to have a regulatory pathway?

Mikael Dolsten - *Pfizer Inc. - Chief Scientific Officer and President of Worldwide Research, Development & Medical*

Yes. I mean we were already running the standard pneumococcal regulatory package that we have been using. It's one larger effectiveness study. It's a lot consistency study to show manufacturing performance, and then we have also studied for patients that would have been immunized with other pneumococcal vaccines that can now get extended coverage. So we expect all of the studies required for filing to be available next year. And likely, we'll move into filing next year, pending positive readout. We feel very confident about the other trial that we're discussing now, and we've been able to move very swiftly with it.

Bo Chen - *Evercore ISI Institutional Equities, Research Division - Research Analyst*

All right. So back to the Prevnar 13 approval in infants. You had 3 serotypes that missed the primary endpoint, the responder rate. However, FDA gave a pass because -- partly because, back then, there were some technical issues with the OPA asset. So with the PCV20 nowadays, do you expect that FDA would be stricter on the criteria for approval-- namely, that you want to have all 13 shared serotypes that meet the non-inferiority space?

Mikael Dolsten - *Pfizer Inc. - Chief Scientific Officer and President of Worldwide Research, Development & Medical*

It's a great question. I think we've got a lot of experience, together with FDA, as we developed the 7 valent, 13 valent. And when you look at the 3 endpoints that we use percent responder at a certain IgG cutoff level geometric in concentration of -- in this case, the 20 versus the 13 and the functional antibody response is really the totality of the data that is the most important thing. And even those that we narrowly missed, the 6, 9 and then with serotype 3., on one of the endpoint, percent IgG, when you then look at GMC and OPA and compare to effectiveness, you could see that there was strong effectiveness for those serotype also in the market. So it really confirmed, I would say, that when you look at the totality of the data, you can predict the effectiveness and not just one single endpoint.

So I think FDA, with all of that experience, is likely going to look at the totality of the data, which we feel very good about because we think we have strong data across the board on this endpoint.

Bo Chen - *Evercore ISI Institutional Equities, Research Division - Research Analyst*

Yes. So what's your current thinking on what causes the immune interference, namely you pack more serotypes into the vaccine than you see the immunogenicity against each serotype would decline?

Mikael Dolsten - *Pfizer Inc. - Chief Scientific Officer and President of Worldwide Research, Development & Medical*

Yes. There's been various speculation about what caused immune interference when you add more serotype. I don't think there is a one good answer that it may some time speculation about carrier suppression, but that's been more for tetanus toxoid as carrier than [CRIM] that we use as a carrier.

So we don't really know what may cause it. Again, when you compare the 13 to the 7, there was a minor reduction in some titers when you looked at assays. But when you looked at performance in immunized patients, the protections seems of similar nature. So I think those minor variations haven't really panned out to have clinical implications. We feel very confident that what we see with the 20-valent is a robust response with immunicity of very favorable safety profile and believe that we will construct like we did with -- we have constructed with adult trial and are planning to do it with the infant trial, Phase 3 of a sample size that will help us to get a very successful outcome from those trials.

Bo Chen - *Evercore ISI Institutional Equities, Research Division - Research Analyst*

One last question on the pneumococcal vaccine. Phase 2 infant when you press release the proof of principle after dose 3. We've got a lot of questions why you chose to press release that early. Why not just wait a few more months to have the post-dose 4 analysis? Because you would need that for the FDA discussions.

Mikael Dolsten - *Pfizer Inc. - Chief Scientific Officer and President of Worldwide Research, Development & Medical*

Yes. It was an internal decision point for proof-of-concept based on the 3 infant immunizations. It actually correlates in effectiveness studies quite well for that vulnerable population with 3 immunizations. The fourth is to boost the vaccine to have a longer-lasting protection. And we now have, obviously, a fourth dose data in our hands as well as functional antibody response. And our confidence remains very high as we see very favorable days data emerging from those data sets.

And it was our experience from previous pneumococcal vaccines that made the internal decision point on 3 doses, and we've decided to communicate them as we were communicating inside the company about the positive readout. And as we have accumulated more data, it's -- the experience we had with the secondary stands very strong here. The data sets continue to look very promising, and we are planning and preparing for end of Phase 2 meeting in order to start Phase 3 trials next year.

Bo Chen - *Evercore ISI Institutional Equities, Research Division - Research Analyst*

Got it. So maybe switch to C. Diff vaccine. Do you agree, in general, that this is a high-risk, high-reward program? And how can we think about the C. diff infection rate that's lower in the Phase 3 when you have the interim. And because, in one hand, when you have a lower infection rate, that may speak to the efficacy of the vaccine. However, we see that Sanofi, before they discontinued their Phase 3 program, they also expanded the trial.

Mikael Dolsten - *Pfizer Inc. - Chief Scientific Officer and President of Worldwide Research, Development & Medical*

Yes. I wouldn't call -- personally, I think it's more a high-complexity, high-reward trial. I don't see the scientific risk at all as high, and that's based on the -- what insignificantly, it's not the bacteria, but the toxins that cause the disease. As you know, there are data now with antibodies for relapsing C. difficile that shows that you can utilize the toxin and prevent the disease for relapsing patients.

So we have been able to design a very sophisticated vaccine using molecular cloning of the 2 toxin and mutagenesis to preserve their antigenic structure while making them atoxic for use in a vaccine. And it was very different from the Sanofi trial, which used a more historical approach by chemical inactivation of the vaccine. And those attempts in our hands have given a very poorly immunogenic vaccine.

We also did significant regimen studies comparing weekly to a monthly schedule. Sanofi used a weekly schedule. We saw a much better response with a monthly schedule.

So I think we did all that detailed work and feel very optimistic about the scientific prospect of the studies. Of course, this is an area of pioneering effort because we have to characterize which patients are at high risk. We have to be able to recruit them into our trial and get an event between

months after the third dose of the 6 months. And we also have to develop unique diagnostic tests to differ patients that may carry C. difficile but doesn't have diarrhea driven by C. difficile. We developed this proprietary cellular toxicity in neutralization cells.

And then finally, it's a complex logistics. Patients have to take stool samples at home and have to send them in under certain conditions. So that's why I said, for me, it's more a high-logistics, medium-risk, very high reward. And we are taking the learnings from the trial before, which we have been executing well and looking at whether we should possibly expand enrollment in order to get events faster because I feel very optimistic about the study. So when you have event-driven studies, you can either wait longer time or expand the population to get faster conclusion of the study. So we're doing those analysis to assess what should be the next step.

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

Got it, got it. Mikael, loaded question. In your tafamidis Phase 3 outcomes trial, 20 and 80 ml -- so when you go from 20 milligram to 80 milligram, TTR stabilization goes up, but outcomes benefit did not go up. There's a competitor out there who believes with the higher TTR stabilization, they could possibly improve upon the survival benefit seen with tafamidis? How do you think about that?

Mikael Dolsten - *Pfizer Inc. - Chief Scientific Officer and President of Worldwide Research, Development & Medical*

We think that 80 milligrams is near maximum stabilization and there were -- were some subgroups of patients that did do better in 80s, and we think it's near maximum. There isn't any evidence that a minor incremental change would have any difference.

We also think that 80 milligram, there's no other oral drug in our hands that can stabilize better than the 80 milligram when you run the assay under proper standardized condition. So we feel very good about the 80 milligram and its robust efficacy, multiple endpoints, including outcome standpoint or mortality and hospitalization for cardiomyopathy patients. And the uptake in physicians has been very strong. And you heard at our previous quarterly report exceeding, I would say, expectation. And we think it's going to continue as it's so well-tolerated a drug, too.

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

Got it. Okay. So there's that. We have Alnylam approaching also the same target but turning the tap off rather than just stabilizing. Should that improve the survival benefit in cardiomyopathy studies from an RNAi approach?

Mikael Dolsten - *Pfizer Inc. - Chief Scientific Officer and President of Worldwide Research, Development & Medical*

I mean that's hard to know. I think one needs to wait for trial. And obviously, the advantage with stabilizers is that even already produced TTR has turned from toxic to tolerable by a stabilizer. So I don't know whether that would be successful. Maybe you could also consider combination of them for patients that have very advanced disease, and that's something we're looking into, but that would be more a subset of the opportunity.

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

Got it. Oral GLP, it sounds like the expectations went up internally, but then there's also now feedback that there's 2 programs in parallel. Perhaps the backup one is better than the first one. Can you catch us up on where you guys...

Mikael Dolsten - *Pfizer Inc. - Chief Scientific Officer and President of Worldwide Research, Development & Medical*

Yes. I heard you were discussing oral GLP when I came in from the door here. We have a very exciting oral GLP-1, the front-runner in our Phase 1b. We saw dramatic reduction in glucose and also in body weight. So the profile we're targeting based on that for diabetes would be to be as good or better than the injectable and substantially better than any oral compound we have seen in the market or in development.

And similarly, for obesity, the data in the smaller trials, if we can reproduce now in a larger Phase 2b study, is aimed to drive very substantial reduction in body weight. The key with oral drugs is that it allows you probably to titrate them for getting some of the optimal dose, easier than the injectable because you have this class intolerabilities of nausea that the patient needs to get used to. And that's really what we have been thinking about for the diabetes, obesity...

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

So why 2 programs? Is their formulation different?

Mikael Dolsten - *Pfizer Inc. - Chief Scientific Officer and President of Worldwide Research, Development & Medical*

Yes. I would say, we -- our main focus is on the front-runner drug. But as we saw in obesity that patients may even benefit from higher doses in -- than in diabetes, and it may be driven by certain characteristics of exposure, while we removed the first drug, we were so intrigued by the potential of having such a strong metabolic drug for 3 indications. We didn't want to miss out on any opportunity then to also have a second with a different PK.

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

Got it.

Bo Chen - *Evercore ISI Institutional Equities, Research Division - Research Analyst*

So one last question on the gene therapy. You recently invested additional $500 million in the facility. Does that facility speak to specific programs in DMD or hemophilia or is it expandable for all potential AAV partnerships?

Mikael Dolsten - *Pfizer Inc. - Chief Scientific Officer and President of Worldwide Research, Development & Medical*

Yes. Great that you asked about it. We have a large capability in North Carolina, both on manufacturing for the market and for clinical studies. And we think that's a very versatile, flexible manufacturing platform. And we will use it also for partnering with smaller companies because we think not just ability to manufacture but an in-depth analytical and purification skills we have had -- we have. And when we compare that with what we get from other companies, we think we can really improve the yield, the purity and the characterization of the product.

So we think it's a competitive advantage, not just for our product, but for companies that wants to partner with Pfizer that may allow them to have an easier and more high-end dialogue with regulators across the globe about this new field and a new type of product.

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

Mikael, DMD, the investor perception is Pfizer is not competitive. Do you agree with that?

Mikael Dolsten - *Pfizer Inc. - Chief Scientific Officer and President of Worldwide Research, Development & Medical*

No. I think we have a very much competitive product with any other data that's been out there. What often happens is that the smaller companies throw a segment data on the table, and I think it was the data initially on -- that some patients may gain a lot functionally, but it's all about the age of the patient. Patients gain spontaneously while treatment in DMD early life, so you have to look at age of the patients. And actually, when we compare the few patients we had, our data stands out very well on all our endpoints.

So it is a tricky area because you need to look at the baseline of the patients, the age of the patients, and then you need to, obviously, look at the numerous type of assays you're using and the clinical functioning data set. So in all, this is obviously an extremely high-reward field with risk because all companies have dosed the limited number of patients. What we have seen so far, we think, is highly competitive. We have expanded the dosing, and we hope to be able to share data early next year with those communities.

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

When would that be?

Mikael Dolsten - *Pfizer Inc. - Chief Scientific Officer and President of Worldwide Research, Development & Medical*

We think first half of next year, we'll have data. And we're planning, actually, to move swiftly into Phase 3 based on our current smaller data sets that we think is very encouraging. Comparing to available data from other companies, we think it's very encouraging.

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

Fascinating. Wow. That will be the highlight of this conference.

All right. Thank you so much for joining us. It was really -- it was a pleasure having you all.

Mikael Dolsten - *Pfizer Inc. - Chief Scientific Officer and President of Worldwide Research, Development & Medical*

Thank you.

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

Thank you.
