Transcript of FDA Press Conference on the Update to the Existing Box Warning on Avandia.

FTD-HHS FDA

Moderator: Susan Cruzan
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Coordinator: Welcome and thank you all for standing by. At this time your lines are on a listen-only mode until the question and answer segment of the call. At that time if you would like to ask a question, please press star 1.

This call is being recorded. If you do have any objections, you may disconnect at this time.

I would now like to turn the call over to Susan Cruzan. Thank you. Ma'am, you may begin.

Susan Cruzan: Good afternoon and thank you all so much for joining us today. This is FDA's Press briefing to discuss an agency announcement on a product safety issue - folks probably know what this is.

I will turn this over to Dr. Woodcock who will make some very brief remarks and then we will open it up to your questions. And again, this is for credentialed media. Thank you. Dr. Woodcock?

Janet Woodcock: Thank you, Susan. What we're today announcing is an update to the existing box warning on Avandia. Of course the black box is the

strongest form of warning and we are adding another statement to that black box.

This warning is based on the meta-analysis that showed a potential increase in cardiac ischemic events or heart attacks and related events in one set of studies - one type of study of Avandia.

The sponsor of this drug, Avandia, is GlaxoSmithKline and we have worked with the sponsor to revise the label of the drug in several ways. In addition, GSK is developing a medication guide for patients to provide additional information about the benefits and risks, and safe use of Avandia so that we make sure that patients will be - have complete information about the benefit/risk profile of this drug.

We are keeping Avandia on the market because we've concluded there isn't enough evidence to indicate that the risk of a heart attack or cardiac ischemia is higher for Avandia than other Types of diabetes treatment.

Therefore, we requested that GSK conduct a long term study to better assess cardiovascular risk of Avandia -- or rosiglitazone is the technical name -- as compared to the other oral anti-diabetic agents.

GSK has agreed and we're working with them right now to ensure this study is started and completed in a timely manner. This whole issue of cardiac ischemia is a complicated one because some short term studies, in others words around six months duration, in this meta-analysis have shown a risk of increased cardiac ischemia.

But three larger clinical studies comparing Avandia to other diabetes treatments that were of longer duration and actually had the same number of patients, did not show a similar finding.

FDA is trying to sort out the reason for the differences in these results, including whether this is due to different study designs, different patient populations, different comparisons, drug was compared to different - to placebo in many of the cases where the harm was show, or the duration of the study.

Two FDA Advisory Committees of external efforts - experts, excuse me, the Metabolism and Endocrine Advisory Committee - and combined with the Drug Safety Advisory Committee -- recently discussed all the available information related to this topic.

They voted that Avandia should not be withdrawn from the market on a 22 to 1 vote, but they recommended that the labeling should be updated to describe the findings from the meta-analysis and the long term study with regard to cardiac ischemia because they felt the data suggested there could be an increased risk.

Following the Advisory Committee Meeting, the FDA staff held a number of internal meetings to determine the path forward regarding our regulatory action. It was clear at the Advisory Committee and subsequently that there were different opinions regarding the appropriate regulatory action.

And therefore, the issue was referred to the Drug Safety Oversight Board for advice. This is an internal Federal Board composed of FDA

employees and other people - Federal employees such as people from NIH and the VA to provide advice on these difficult issues.

This Board was split in its vote, but overall felt that the drug should stay on the market and their recommendation was given to the Center Director.

So following these extensive analyses and deliberations that have been done, both in the Public Advisory Committee and internally, and multiple discussions, we have determined that these are the proper decisions to be made at this time.

People with Type 2 diabetes who have underlying heart disease or are at a high risk of heart disease should talk with their healthcare providers about the revised warning as they evaluate their treatment options for diabetes.

And FDA is advising healthcare providers to closely monitor patients who take rosiglitazone for congestive heart failure that has been in the drug label for - in the black box for quite some time as well as other cardiac ischemic symptoms on that warning has been added.

So that was a lot of talking. I think I will now open this up for questions.

Susan Cruzan: We can have the first question, please.

Coordinator: Peggy Peck, you may ask your question and please state your organization.

Peggy Peck: Yes, this is Peggy Peck with MedPage Today. And I'm wondering if you could just read the specific change in the label? And also I have a follow-up question.

Janet Woodcock: Well I think it will soon be posted on the Web. Okay? But the label black box says, "A meta-analysis of 42 clinical studies (mean duration 6 months; 14,237 total patients), most of which compared Avandia to placebo, showed Avandia to be associated with an increased risk of myocardial ischemic events such as angina or myocardial infarction. Three other studies (mean duration 41 months; 14,067 patients), comparing Avandia to some other approved oral antidiabetic agents or placebo, have not confirmed or excluded this risk. In their entirety, the available data on the risk of myocardial ischemia are inconclusive."

And this is - basically lines up with what the Advisory Committee told us and that is in the Press Release.

Peggy Peck: Okay. And my - and on follow, in your opening remarks you stated that one of the reasons that the decision was made to leave the drug on the market (unintelligible) shown that there was a (unintelligible) additional risk, an excess risk with this drug.

So my question then is if there is no excess risk, should not other drugs in the class also have this language added?

Janet Woodcock: This drug has never been directly compared head-to-head with the other - only single other existing drug in the class - piaglitazone. However, most diabetics are started on metformin or a sulfonylurea and the data that we have comparing these against this drug do not show differences.

Peggy Peck: Thank you.

Janet Woodcock: Mary Parks is also on the line. Mary, if you have any comments on any of my comments on diabetic therapy, please jump in.

Mary Parks: Okay, I think that that covers it, Dr. Woodcock.

Coordinator: Our next question is from Rita Rubin. You may ask your question and please state your affiliation.

Rita Rubin: Hi, Rita Rubin from USA Today. I have two questions. One, Dr. Woodcock you mentioned the Drug Safety Board was split. Were they split on whether to stay on the market? And if so, how split were they?

And my other question was the study that Glaxo has agreed to do, I'm a little unclear. Is it comparing it only to Actos or is it comparing it to other oral antidiabetic drugs as well?

And why have you not like gone to the manufacturer of Actos and say, you know, we want to see a study - we want to see you do a study looking at your drug's risk of ischemia?

Janet Woodcock: Okay. First just let me say who else is on this call from the technical side besides me. Dr. John Jenkins who is the head of New Drugs, is here. Dr. Mark Avigan who is within the Office of Surveillance and Epidemiology, and Dr. Mary Parks, who is the Division Director of the Metabolic and Endocrine Division are also on the phone with me.

And they are more expert on many of these matters than I am. For the first question about piaglitazone, that manufacturer has conducted a study in a different population of patients who are at risk of cardiovascular disease which has been a fairly long term study and did not reveal an increased risk. Okay?

With regard to what study we're asking GSK to do, we are still in negotiations about that and Dr. Jenkins or Dr. Parks may wish to add more.

John Jenkins: Yeah, this is John Jenkins. We have reached agreement with GSK that they will conduct a study in the timeline for the conduct of the study.

Some of the fine point details about the comparison groups and other aspects still need to be discussed and agreed to. Those have not been finalized yet.

Rita Rubin: So you don't know - you're not sure what the compare to drugs are going to be yet?

John Jenkins: We clearly expect piaglitazone to be one of the comparators, but the natural history of diabetes is that patients eventually move on to require more than one therapy.

So even if you've started the study initially as just head-to-head comparing one drug to a single other drug over the course of time, many of those patients will need other drugs added to help control their diabetes.

So this will likely be, you know, a long term study. It could take as many as four or five years. So over that time it'll be multiple comparisons.

Rita Rubin: Is it a randomized trial that you're talking about?

John Jenkins: Yes.

Rita Rubin: Okay.

Mary Parks: Hi, this is Dr. Mary Parks. The other thing that I would add here is that currently none of the approved oral antidiabetic therapies have demonstrated that they can reduce cardiovascular risk.

And as Dr. Jenkins had noted, these trials would take a very long time to conduct and because the complexity of the disease requiring multiple therapy over the years, it's very important to make sure that the appropriate adequate study and adequate comparators are selected.

And this echoes what Dr. Woodcock had discussed as to the label and the decisions made on this product here, is that at - when the study is concluded we want to make sure that it was the right study, right design and right comparators to give us more definitive answers.

Susan Cruzan: Thank you. We need to move on to the next question, please.

Coordinator: Jennifer Corbett, you may ask your question and please state your organization.

Jennifer Corbett: Yeah, I'm Jennifer with Dow Jones. The question I have is I'm assuming that the new warning would also apply to the other drugs - the combination drugs, you know, that contain Avandia?

Janet Woodcock: Dr. Parks?

Mary Parks: That is correct.

Jennifer Corbett: You know, Avandamet and - okay.

Mary Parks: That is correct. Avandamet and Avandaryl will also contain this.

Jennifer Corbett: Okay, thank you.

Susan Cruzan: Next question, please.

Coordinator: Daniel DeNoon, you may ask your question and state your organization.

Daniel DeNoon: Thank you. I'm Dan DeNoon with WebMD. I'm - with all this I'm a little confused now. So am I understanding this correctly that this is the first label change to address a heart attack, not the earlier heart failure warning?

This is the first change to attack - to address the panel advisories? And if that is true, then is this exactly what the panel recommended or in what ways is it different?

Janet Woodcock: Dr. Jenkins?

John Jenkins: This is Dr. Jenkins. This is the first labeling change since the Advisory Committee in July of this year. There was a labeling change, I believe in June of 2006 that did address some early findings from a single study about possible increased myocardial ischemia.

I forgot the last of your question.

Woman: (Unintelligible).

John Jenkins: The Advisory Committee - they also struggled with the issue. If you look at the vote, they voted pretty strongly in favor of the question about whether the study suggested an increased risk of myocardial ischemia.

Some of them felt like it was very difficult to know for sure that there was an increased risk. And then they voted to maintain the product on the market. As Dr. Woodcock said earlier, I think the vote was 22 to 1.

So in many ways we think the labeling changes are consistent with the Advisory Committee votes and recommendations.

Susan Cruzan: Can we have the next question, please?

Coordinator: David Brown, you may ask your question and please state your affiliation.

David Brown: Yeah, it's David Brown with the Washington Post. I am also a little bit confused. The - is the current belief that there is equal cardiovascular risk between Avandia, sulfonylureas and metformin?

And is the implication that if one of them - if they don't all ultimately turn out to have equal risk when they are put head-to-head with each other in this planned study, that unless they're all equal, than the higher one immediately gets bumped off the market - that that is a - that that is by definition for not an acceptable state of affairs to have one that's higher than the others in terms of cardiovascular risk?

Janet Woodcock: Let me start. This is Janet Woodcock and then I'll turn it over to Dr. Jenkins. The sulfonylureas have had a black box warning since what, the 70s I think, about cardiovascular - risk of cardiovascular death. Okay?

So those have long been under some question about whether - based on trial data about whether they raise the risk. The reason that we made the statement that we don't think that - we don't have evidence that this drug increases the risk compared to other antidiabetic drugs is because of the data that we have in front of us. That's what the data show.

The question about whether if one had a slightly increased risk over another of cardiovascular problems, first of all a very small risk would be very hard to be (unintelligible) even a very big trial.

Second of all, don't forget all of these have other liabilities. All drugs have a variety of benefits and risks associated with them, which (unintelligible). So a benefit/risk analysis (unintelligible) or a risk (unintelligible) drug.

So let me (unintelligible) to Dr. Jenkins (unintelligible).

John Jenkins: Yeah, a couple of things to emphasize in looking at the data, the meta-analysis of the 42 clinical studies did seem to show an increased risk of myocardial ischemia, including things such as myocardial infarction.

As we looked at those data, it seemed like much of the difference was being seen in studies where Avandia was compared to placebo. When we looked at the longer term studies, the three long term studies that were discussed at the Advisory Committee where Avandia was compared to other active therapies, a similar finding was not observed.

And in fact, in some of those studies the overall mortality, the overall number of deaths tended to favor those patients randomized to receive Avandia. So the overall message we have is we have a signal from the short term trials that were included in the meta-analysis.

It was largely driven by comparison to placebo. When we looked within the meta-analysis or across the large studies, when we compared to other oral antidiabetic agents, we don't see the same findings.

And that's why we've reached the conclusion we have. You know, I think it's important to understand that patients with diabetes need therapies. So placebo is not an option for long term care for patients with diabetes.

So as we look at these data, we really need to understand the risk of the drug and the benefits compared to the other available therapies.

David Brown: Okay, can I just have one follow-up? So can we conclude that the planned study will be a head-to-head study of Avandia versus metformin and at least one sulfonylurea?

John Jenkins: As I said earlier, the absolute details of that have not been finalized. We clearly want to see piaglitazone included as one of the comparators in that study and I'll see if Dr. Parks wants to say anything further about what we expect the design to be as far as comparators?

Susan Cruzan: Dr. Parks?

Mary Parks: The only thing I would add is just a clarification with regard to the labeling from sulfonylurea. As Dr. Woodcock pointed out, this was actually in place many, many years ago after the UDPD study about 20 years ago.

It's actually not a box warning, but it's a very prominent (golded) language under the warning section.

Janet Woodcock: Oh, sorry Mary.

Mary Parks: That's okay. And it's for cardiovascular mortality.

Janet Woodcock: Right.

Susan Cruzan: Can we have the next question, please?

Coordinator: Christopher Kelly, you may ask your question and please state your organization.

Christopher Kelly: Yeah, this is Chris Kelly with FDA, our gathered news media here have no further questions. Thanks.

Susan Cruzan: Do we have another question, please?

Coordinator: Ricardo Alonso-Zaldivar, you may ask your question and please state your organization.

Ricardo Alonso-Zaldivar: Hi, I'm with the LA Times and thanks for taking my question. I wanted to get back to Rita Rubin's question. What was the question that was put to the Drug Safety Board and what was the vote of the Drug Safety Board?

And I have a follow-up, thank you.

Janet Woodcock: Yeah, the vote was split. I'm not going to go into the numbers. I don't remember the numbers, but it was split. And remember, various parties from all different points of view had different opinions. It wasn't split along any what you might call predictable line.

Susan Cruzan: Do you have a follow-up?

Ricardo Alonso-Zaldivar: Yeah, I do. That - when you say it was split, what was it 50/50 or something like that or was there a majority for keeping the drug on the market?

Janet Woodcock: Yes there was an authority for keeping the drug on the market.

Ricardo Alonso-Zaldivar: Okay. And my follow-up question is why didn't FDA go with the advice of its Drug Safety Office on this? You had Dr. Graham and Dr. Dalpan both saying the drug should be withdrawn.

And you think this - you'll run the risk here of being accused of undercutting your own Drug Safety Office again? Could I have your comment on that?

Janet Woodcock: We took into account a very broad variety of opinions. We've had our external advisors, our Risk Management Committee, our Safety Committee, Advisory Committee as well as the Endocrine Committee weighed in upon this.

They gave us some opinions. We had a process whereby we went over all the recommendations internally of the various parties and various scientists who had reviewed all the different data.

This was also looked at by the Drug Safety Board internally and overall a decision had to be made about which way to go. And so based on the evidence and data as we have laid out in the label and everything, this was the decision that was made.

Ricardo Alonso-Zaldivar: Okay. But - so you don't think that you're going to be accused of undercutting your own safety advisors again? Or you're confident that maybe their mistaken?

Susan Cruzan: No, Ricardo, I think we answered your question and we need to move on. Thank you.

Coordinator: (Unintelligible), you may ask your question and please state your organization. Please check your mute button, sir. (Red No), your line is open. I'm going to move…

Susan Cruzan: Are you there?

Coordinator: Please check your mute button, sir.

Susan Cruzan: All right. If you're not there, we can move on.

Coordinator: Okay. (Cathy Hollingsworth), you may ask your question and please state your organization.

(Cathy Hollingsworth): My question has been answered sort of about the Drug Safety vote.

Susan Cruzan: I'm sorry, what was the question?

Janet Woodcock: That it was answered about the vote.

(Cathy Hollingsworth): My question was sort of answered already, so…

Susan Cruzan: Okay, can we have the next question please?

Coordinator: Gardiner Harris you may ask your question and please state your organization.

Gardiner Harris: I'm with the New York Times. Just quickly, I'm a little confused about the difference in the labels between pia and rosiglitazone because I think in the Press Release it said that all other oral antidiabetic agents will have to say that they do not have any evidence about their effect on ischemic risks.

But you do have some evidence from piaglitazone, I believe. So help me to - what's going to be on the piaglitazone label? Is it going to be

this standard mention that there is not any evidence versus in heart risks or will there be no change to the piaglitazone label as a result of this?

What are the differences between these two drugs going to be?

John Jenkins: Yeah, this is Dr. Jenkins. As we stated in the Press Release, we plan to ask all the manufacturers of the oral antidiabetic medications to add the statement that you're referencing that says to date no oral anti-diabetes drugs have been conclusively shown to reduce cardiovascular risk.

The piaglitazone labeling includes information about the proactive study that was done as an outcome study. Our review and interpretation of that study and as it's labeled, was that it did not show conclusive evidence of reduced cardiovascular risk.

There were some trends that were discussed at the Advisory Committee but the study on its primary end point did not show a reduction in cardiovascular risk so we expect that they will have the statement that I read earlier.

Gardiner Harris: So it will have that statement but it will not have the statement that you're going to be asking that Avandia have? So that's going to be a clear difference then?

John Jenkins: Well Avandia will have the box warning which we approved today, that Dr. Woodcock read earlier. Clearly there's been a signal of concern raised for Avandia from the meta-analysis as we say on the box.

If we look at all of the data in their entirety, the available data on the risk of myocardial ischemia are inconclusive. So we want to make sure that healthcare providers and patients are aware that this signal of a risk has been identified and while we're waiting for the more definitive studies to be completed, make sure that they take that into account as they make their decisions.

But we also want to add to the labeling of the other agents a statement to make clear that none of them have been conclusively shown to reduce cardiovascular risk.

Janet Woodcock: Yeah, one - Gardiner, this is Janet Woodcock. One is about reducing the risk of cardiovascular disease which has to do with intensive treatment of diabetes and so forth and so on.

The other is whether a risk, you know, an additive risk, an increased risk occurs. So that's the difference. As many of you know, some of the anti-diabetic - diabetics are now treated intensively trying to control their blood sugar very closely in order to (foresaw) many different types of complications such as blindness, kidney failure and so forth and so on.

Cardiac ischemic complications, though, have not been shown to be reduced by this although there's some thought in the community of course that it certainly could be a factor.

Susan Cruzan: Thank you. We'll take about three more questions. Could we have the next question please?

Coordinator: (Ann Matthews), you may ask your question and state your organization.

(Ann Matthews): Hi, I'm with the Wall Street Journal. Could you describe for us a little bit of the process that led to this language in the label? I was curious what FDA had originally proposed. I don't know if you can share details.

But - and how different this is from that? Was there a process of negotiation with the sponsor that led to this language and is this language close to what the FDA would have wanted on its own? Or how is it different, if different?

Janet Woodcock: I would say we are comfortable with the language, but I can't - I'm not going to be discussing the - we wouldn't have approved the label if we weren't comfortable with the language.

But we're not going to be discussing the back and forth that we have. We always have discussions that - what goes in any part of a label.

John Jenkins: And this is John Jenkins. I would add to that that all of the members of the team that were involved in reviewing the information were involved in the discussions internally about what the wording of the boxed…

Janet Woodcock: Yeah.

John Jenkins: …warning should include. So that included Dr. Dalpan, Dr. Graham and others. They were all involved in decisions about what the wording should be.

(Ann Matthews): And Dr. Woodcock, I think, had mentioned that it had been clear that there were different opinions about the drug among FDA staff. Were there still different opinions when this decision was reached or was there a - did everyone sort of agree as this is the right thing to do?

Janet Woodcock: Well I'm not going to speak for everyone. We certainly made a decision how we were going to go forward, how people then started working on crafting the label as John said, and are working the design of the studies.

There certainly - there's a lot of uncertainty around this as is many other decisions that we made and individuals can come out on either side of the question. And they are encouraged and expected to voice their own scientific opinions, okay?

So we don't expect everyone to, you know, agree at the end of the day. But we make a decision based on the best possible scientific data and then we move forward. And that's what we're doing in this case.

Susan Cruzan: Thank you so much. We need to take the next question.

Coordinator: Michelle Cortez, you may ask your question and please state your organization.

Michelle Cortez: Bloomberg News. I wanted to come back to the Actos question again. So basically just making sure that I understand what you're saying - that Avandia hasn't been shown to have increased risk compared to other cardio- other diabetes drugs, namely metformin and the sulfonylureas.

But Actos has been shown to not have increased risk in the study - the proactive trial that they were done. Is that correct?

John Jenkins: This is Dr. Jenkins. That's not entirely correct. The proactive study was a cardiovascular outcome study comparing piaglitazone to other antidiabetic agents. That study did not meet its primary objective, which was to show that piaglitazone had more favorable outcomes.

So to say that it - there was not a signal there of increased risk. That's true, but that's not a conclusive finding just as it was not conclusive that it decreased the risk either.

Michelle Cortez: So there doesn't need to be a black box warning on pia saying that it has the same risk as Avandia because of the proactive trial? Or is that still an open question because you're asking them to do this comparative head-to-head trial?

John Jenkins: Piaglitazone has the box warning for congestive heart failure. At this time they do not have a box warning for myocardial ischemia.

Michelle Cortez: And so is there a way to categorize if there's a difference between these two drugs when it comes to the myocardial ischemia issue?

John Jenkins: Well as I said earlier, we had the signal from the meta-analysis that suggested that patients receiving Avandia -- rosiglitazone -- might be at increased risk of myocardial ischemia.

As we've looked at all the data, we still have that signal from the meta-analysis, but we haven't been able to confirm that observation or refute that observation when we look at the database in its entirety.

So it's still an open question for Avandia and that's why we've asked Glaxo to do the long term study that we discussed earlier.

Michelle Cortez: Right. I'm asking a very narrow question. Perhaps I'm not doing it clearly enough because in the Press Release you guys put out you said that there is not yet conclusive data that Avandia has a greater risk than other cardiovascular drugs.

And I'm just wondering whether that other cardiovascular drugs includes pia?

John Jenkins: That would include pia, yes. I'm sorry if I didn't understand your question earlier. But I think as Dr. Woodcock said, the number of studies of head-to-head comparisons of rosiglitazone to piaglitazone - there's only a few and they've been very small.

So they would not be an adequate basis to make any findings about the comparison between those two drugs.

Susan Cruzan: Okay, thank you. We have time for one more question.

Coordinator: Chris Hollis, you may ask your question and state your organization.

Chris Hollis: Hi, FDA News. Pardon me if this has been said before. Timelines on the study - it was said four to five years it could take. I wanted to see if there were any defined timelines of when the agency would see data before the study was fully completed.

John Jenkins: This is Dr. Jenkins. We typically, in letters where we talk about post-marketing study commitments, put in milestone dates for when we expect certain events to have occurred. And we did that in this study.

We expect the final protocol for the study to be submitted to the FDA by the end of July. We expect the study to start by the end of November. And we expect the final study report to come to us by the end of March 2014.

Janet Woodcock: But of course for those on the phone who may be not aware of this, there would be interim data probably during this time period where we would either be reassured or have to drop certain drugs or whatever depending on what the findings were.

And that will be built into the protocol as well. So it isn't as if we're going to be clueless until 2014.

John Jenkins: That's true.

Janet Woodcock: However, it would take until 2014 to completely do this and determine these drugs are equivalent anyway.

John Jenkins: And let me expand on that a little bit because people not involved in large clinical trials may find some of these timelines to be surprising. There's a lot of work that needs to go into developing the protocol and getting all of those issues sorted out about the comparators, the patients that will enrolled, the enrollment criteria - those types of issues.

That's why it takes months to develop a protocol and then FDA will have to review the protocol and come to agreement with the sponsor on the protocol.

So we're saying that the final protocol will be submitted no later than July 31, 2008. It could be done earlier than that, but that's a reasonable timeframe for this type of study.

Once the protocol is agreed between FDA and the sponsor, there's still a lot of work that needs to occur before patients can actually be enrolled, including IRB approval at the local sites, recruitment of investigators, recruitment of patients.

So that's why we wouldn't expect the first patient to be enrolled until several months after the protocol is agreed between FDA and GSK.

And then finally, this study -- like all cardiovascular outcome studies -- will be monitored by an independent data safety monitoring committee and they will have stopping rules to stop the study early if they're starting to see an adverse finding in one direction or the other as Dr. Woodcock suggested.

So the final study report would be submitted to FDA by 2014 as I described. But we would certainly expect to hear about the study as it's ongoing, in particular if they're seeing an adverse finding.

Janet Woodcock: In one - in any area compared to another area, right?

Susan Cruzan: Okay, with that - that concludes our call today. I just wanted to thank our FDA folks, Dr. Woodcock, Dr. Jenkins, Dr. Parks and Dr. Avigan.

Thank you all and have a great day.

Coordinator: This concludes today’s conference. Thank you.

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