

# FINAL TRANSCRIPT

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**ADDXF.PK - ADDEX PHARMACEUTICALS LTD ADX10059-204 GERD  
Monotherapy Data**

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Nov. 16. 2009 / 3:00PM, ADDXF.PK - ADDEX PHARMACEUTICALS LTD ADX10059-204 GERD Monotherapy Data

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**Vincent Mutel**

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## CONFERENCE CALL PARTICIPANTS

**Mike Aitkenhead**

*Piper Jaffray - Analyst*

**Peter Welford**

*Jefferies - Analyst*

**Olav Zilian**

*Helvea - Analyst*

## PRESENTATION

**Operator**

Good afternoon. I am Moira, the conference call operator for this conference. Welcome to the Addex ADX10059 Monotherapy is Effective on GERD Symptoms in Phase IIb Clinical Trial Conference Call and live webcast. Please note that for the duration of the presentation all participants will be in listen-only mode, and the conference is being recorded.

(Operator Instructions)

This call may not be recorded for publication or broadcast. At this time, I would like to turn the conference over to Mr. Chris Maggos, head of Investor Relations and Communications of Addex Pharmaceuticals. Please go ahead, sir.

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**Chris Maggos** - *Addex Pharmaceuticals - Head of IR and Corporate Communications*

Thank you, and welcome to everyone. We're glad you could join us. Today our Chief Medical Officer, Charlotte Keyword, is going to present the data released this morning in a press release. And then Vincent Mutel, our CEO, will give some remarks regarding the Addex strategy. Tim Dyer, the CFO, is also here to answer your questions.

Charlotte?

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**Charlotte Keyword** - *Addex Pharmaceuticals - CMO*

Thank you, Chris. Good afternoon, everybody. Yes, it gives me great pleasure to present to you today the initial top line data of the major efficacy results for our first study in gastroesophageal reflux disease. The first slide recapitulates as to why we're looking at GERD with mGluR5 inhibition. I think most of you who are on the call are now fairly familiar with that. But really, we're looking at the mGluR5 receptor and its control over lower esophageal sphincter function. And that was really the subject of the study that we've just conducted that I'm going to present to you.

The study we did was a monotherapy study, so we were looking at the effect of giving ADX10059 on symptom control in patients who are known to have gastroesophageal reflux disease -- patients who have classic gastroesophageal reflux disease. They



Nov. 16. 2009 / 3:00PM, ADDXF.PK - ADDEX PHARMACEUTICALS LTD ADX10059-204 GERD Monotherapy Data

were patients who were good responders to PPIs, and we selected those patients especially so that we knew that they had classical GERD and didn't have any form of other type of heartburn or non-typical symptoms.

The patients were taken off their PPIs for a two-week period prior to randomization. And if they had a significant symptom burden once they had withdrawn from their acid suppressant therapy, they were eligible for randomization. And they were randomized to active treatment, 120 mg twice daily, or placebo in a one to one randomization. Of course, the study was double-blind and randomized.

Patients were treated for two weeks and the outcome measures we looked at were the incidence of GERD symptoms in the weeks -- in the two weeks following treatment. And the primary endpoint was GERD symptom free days in week two of treatment. And when I talk about GERD symptom free, that is heartburn and/or regurgitation, so it was a composite of heartburn plus or minus regurgitation.

Other things we looked at were specifics on individual GERD symptoms; heartburn individually and regurgitation individually. We also looked at the number of nights that the patients described sleep disturbance due to GERD symptoms, how often they needed to use antacid rescue medications throughout the study, and also we asked the patients for their global assessment of the study medication. And we also used a GERD symptom questionnaire, which the patient reported outcome, to look at their evaluation on general symptoms of GERD.

The whole study included 90 patients, but in a subset of 24 patients we also looked at mechanistic parameters. We wanted, again, to get more information on reflux events and lower esophageal sphincter function. If you remember, in two previous studies we demonstrated that 10059 does inhibit reflux events and we wanted to explore that again more thoroughly in these GERD patients, and try and see how reflux events might correlate with GERD symptom control.

So if we go to the next slide, and this is the primary endpoint, we're looking at symptom free days comparison of active versus placebo, taking into account the baseline symptom burden. And as you can see, there was quite -- there were very few, I should say, symptom free days in the baseline period, 0.46 for the 10059 group and 0.72 days for the placebo group. We required the patients to have significant symptoms having withdrawn from their PPIs in the baseline period.

And this increased quite markedly to 2.5 days in the 10059 group and 1.71 days in the placebo group. We saw a difference of approximately one day of 10059 over placebo. So, the patients who take ADX10059 on average had one more symptom free day at week two of treatment compared to baseline, and this was statistically significant.

If we look at the mechanistic primary efficacy endpoint, we look at the all reflux events. Now, with the impedance monitor what you do is you measure resistance in the esophagus by means of a probe that can detect liquid and gas flowing up and down through the esophagus.

And we looked at all reflux events, so that includes acidic reflux events, non-acidic reflux, and weekly acidic reflux; it's a mixture of all types of reflux going on there. And we also looked at, for example, acidic reflux events and weekly acidic reflux events.

So if we look for the first endpoint is the all reflux events. And as you can see, there was a similar level of reflux events in the 10059 and placebo groups, 64.9, 65 on average for 10059 and 77 for placebo. But there was quite a substantial drop at the end of treatment in the 10059 group to 47.9 reflux events over 24 hours, and that compares with no change at all in the placebo group. And that was statistically significant. So, we showed that 10059 reduced the occurrence of all types of reflux events.

Now, the majority of the reflux events that were experienced throughout the 24-hour period were, in fact, acidic reflux events. Don't forget these patients were not on acid suppressant therapy so they had normal stomach acid. So you might anticipate, of course, that their reflux events would be primarily acidic, and indeed they were. And as you can see, in the 24 hours in the baseline period they had a similar number of acidic reflux events throughout that period.



Nov. 16. 2009 / 3:00PM, ADDXF.PK - ADDEX PHARMACEUTICALS LTD ADX10059-204 GERD Monotherapy Data

And again, after treatment with ADX10059, a very substantial drop in the number of acidic reflux events through the 24-hour monitoring period compared with really little or no change for placebo. And again, that was statistically significant.

Moving to the next slide, we looked at a constellation of secondary endpoints, and really these are the headline data. The whole dataset is undergoing further analysis at the moment, so these are really just the headline results from that. So we showed once again that 10059 reduced impedance measured reflux events, and increased the number of GERD symptom free days.

But in addition, treatment with 10059 also increased heartburn free days in week two and in the overall period. It also reduced the number of nights for sleep disturbance and, in fact, we measured it the other way round, we said number of nights with no sleep disturbance. So, 10059 significantly increased the number of nights with no sleep disturbance due to GERD.

And because, of course, patients were getting less in the way of symptoms of GERD, they used less antacid medications. So, there was a significant reduction in the requirement for antacid rescue medication in the patients who took ADX10059.

When we administered the patient reported outcome, which looks at different facets of GERD -- looks at things like upper abdominal pain, lower abdominal pain, symptoms of heartburn, regurgitation, bloating, et cetera. The whole patient reported outcome symptoms score was significantly improved by ADX10059. And certain subscales of that, including heartburn regurgitation, were also significantly improved by the use of 10059.

And these sort of more objective measures and patient reported measures resulted in the patients themselves expressing a significant preference for 10059 compared to placebo. More patients rated the product as good or excellent compared to those taking placebo. So the product, at least in these top line data, appears to be effective and confer a meaningful clinical benefit to patients in this short term study.

Now, an important part, of course, of the use of the product is safety and tolerability and these were evaluated during this two-week study. Firstly, there were no change -- significant changes in any of the safety monitoring parameters, so that's blood test, ECGs, blood pressure, physical signs. And also we looked at the tolerability profile. And, in general the product was very well tolerated.

We saw a few more side effects in the ADX10059 group than in the placebo group, which would of course be anticipated because it's a CNS drug. But over two-thirds of the adverse events in both treatment groups were described as mild and none of them were severe, and none of the adverse events were treatment limiting. So, in fact, the tolerability profile that we achieved with this -- the modified release formulation at this dose in the two-week study seems to be compatible for the use in GERD in this population.

That's the first of the two studies. Of course, as you know, there's another study going on at the moment which we're looking at the -- probably the major use of the product, which is add-on therapy to PPIs. That study's making good progress in the United States and Europe. As you know, enrollment in that study has completed. And we are looking forward to being able to report the results very early next year.

That study is looking at the effect on GERD symptom control in patients who are on PPIs but still have significant breakthrough symptoms. And in this study we are going to be testing three different doses of 10059 versus placebo. Again, it's a double-blind, randomized, dose range finding study. The outcome measures will be rather similar to those that we've used in the current study.

The treatment duration is longer than that we have in the current study; it's a four-week treatment duration instead of a two-week treatment duration. And we will be evaluating the effects on GERD symptom control and the other parameters that I have described to you in the monotherapy study. However, these patients are -- will not undergo mechanistic monitoring in that study; it's purely a clinical symptom control study.



Nov. 16. 2009 / 3:00PM, ADDXF.PK - ADDEX PHARMACEUTICALS LTD ADX10059-204 GERD Monotherapy Data

So, as I say, very interesting news for now; it certainly supports everything we've seen in the past, and we shall look forward to getting additional data very early next year.

Do you have any -- I'll hand over to Vincent.

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**Vincent Mutel** - *Addex Pharmaceuticals* - CEO

Yes, okay. Thanks very much, Charlotte. I think the very important aspect of the development --. I will conclude the talk and I will come back and take question. I think it's partly easier this way. So thanks again, Charlotte. This is a great achievement for the Company. We are very happy to see the efficacy of the drug that we have move forward after these years.

But I think what is very important is to see that this compound really differentiated very well compared to the PPI. We have effect on reflux which is not controlled by the PPI. We have effect on the nocturnal reflux as well and the report from the patients. So, I think here we have a highly differentiated product compared to what is existing, and I think the study showed that very, very nicely and very clearly.

So as we said in the press release, we will continue the development of this molecule for GERD. We believe that now we have a lot of the evidence that we were looking for on the mechanistic standpoint to differentiate the product, and for sure we actively will be looking for a partner.

The compound is still continuing development for migraine prophylaxis, which is an important aspect of the potential out-licensing of this product because for sure it will add a lot of value to the molecule. And, in term of negotiation and discussion with potential partners, this aspect of the potential of the drug is very important as well.

In the meantime we continue the development of 48621, which has completed now the tests we wanted to perform in monkeys. We certainly will announce these result very soon; they are quite interesting. And so we hope as well that this is going to trigger a further development for this molecule, and clearly as well a potential out-licensing as soon as possible.

And for the rest, we have moved our products and programs according to timelines; there's no particular change. We have here a slide with the pipeline in clinical and preclinical development. And on the next slide we have the program in discovery which are moving very well and very strongly.

We have announce at the R&D Day the nature of additional programs in inflammation and metabolic disorder and CNS and they are all moving according to timelines, including our partnership. And we hope to be able to announce good news as soon as possible.

And on that, I will conclude my talk and say again how excited we are and happy we are to have obtained these results and which are opening a lot of possibilities and potential for our company.

Thanks for your attention, and we open now the discussion for questions.

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## QUESTIONS AND ANSWERS

### Operator

We will now begin the question and answer session.

(Operator Instructions)



Nov. 16. 2009 / 3:00PM, ADDXF.PK - ADDEX PHARMACEUTICALS LTD ADX10059-204 GERD Monotherapy Data

The first question is from Mr. Mike Aitkenhead from Piper Jaffray. Please go ahead, sir.

**Mike Aitkenhead** - Piper Jaffray - Analyst

Hi. Good afternoon, and congratulations on the data. I just have one question related to the side effects of ADX10059. Can you provide us with some more detail on the CNS side effects that were seen, specifically the rates of dizziness that were seen with the drug and that of placebo? I'm just trying to get comfort that the sort of side effect profile we saw in the Phase IIa trial hasn't been replicated in the Phase IIb.

**Charlotte Keyword** - Addex Pharmaceuticals - CMO

Yes, as you say, we had -- we did see some mild dizziness in this study as well and it was much lower than we'd seen in the Phase IIa study. So in this study we had an incidence of about 15% dizziness, as I say, most of which was -- or nearly all was mild, and that would respond to about 3% in the placebo group.

So it was slightly higher -- or it was higher than placebo. But overall, looking at the tolerability profile and comparing across all data sets that I have, the tolerability profile in this study looks quite different to what we'd seen previously in the Phase IIa program.

**Mike Aitkenhead** - Piper Jaffray - Analyst

Okay. And just to follow on from that, just beyond dizziness, were there any other side effects of particular note, i.e. percentages of, say, more than 3% to 5% versus placebo?

**Charlotte Keyword** - Addex Pharmaceuticals - CMO

There are not too many. I think it was sleep disorder and vertigo were the other two that were higher than placebo. But then placebo had a higher instance of headache, for example, than active medication. So again, none of those was higher than what we saw for dizziness. And as I say, all of these were -- largely were mild and did not cause interruption of use of the study medication.

**Mike Aitkenhead** - Piper Jaffray - Analyst

Okay. And sorry to push on this, could you give us the percentages for the vertigo and the sleep disturbance versus placebo?

**Charlotte Keyword** - Addex Pharmaceuticals - CMO

I'd have to look for that, actually. I haven't got it in front of me at the moment. But it's -- no, I have to come back to you on that because I don't have the placebo numbers. Got 8% sleep disorder, but I don't have the corresponding figure for placebo.

**Mike Aitkenhead** - Piper Jaffray - Analyst

Okay, thanks.

Nov. 16. 2009 / 3:00PM, ADDXF.PK - ADDEX PHARMACEUTICALS LTD ADX10059-204 GERD Monotherapy Data

**Operator**

The next question is from Mr. Peter Welford from Jefferies. Please go ahead, sir.

**Peter Welford** - *Jefferies - Analyst*

Hi. Two questions on the efficacy of this trial. Firstly, is the efficacy or does -- any tolerance, I guess, that builds up or how rapidly does the drug have an onset, I guess? So what was the sort of trend in those variables over the duration of the two weeks of the study?

And then secondly, on when you look at these data, was there any sort of disparities between patients or is the response -- how tightly grouped are the efficacy across the different patient subsets relative to placebo? Does it look to be certain patients respond better than others potentially?

**Charlotte Keyword** - *Addex Pharmaceuticals - CMO*

Okay, thank you, Peter. In fact, the split from placebo occurs after week one. So, in fact, you see increasing effect of 10059 through treatment. So the number of symptom free days increased more in week two compared to placebo than in week one.

So, you can anticipate as time goes on you would have an increasing treatment effect compared to placebo, and that will be quite interesting to see in our four-week study. So the answer to your question is no, there's certainly not tolerance. In fact, if anything, there's an increasing treatment effect as time goes on.

The second question, we looked at a number of covariates and those are still being analyzed at the moment. So, there's nothing that jumps out of the pack at the moment as being of particular difference between patient types, if you like. The patients are a fairly homogeneous population because we selected them that way because it's a Phase II study. But we are looking at covariates at the moment, but nothing jumps out between the different patient types, like men and women, for example.

**Peter Welford** - *Jefferies - Analyst*

Okay, that's great. Thank you.

**Operator**

The next question is from Mr. Olav Zilian from Helvea. Please go ahead, sir.

**Olav Zilian** - *Helvea - Analyst*

Hello. Thanks for taking my question. And congratulations to these excellent set of data. So did I hear correctly that the headache rate in the placebo group was actually larger than in the 59 group?

**Charlotte Keyword** - *Addex Pharmaceuticals - CMO*

Marginally, yes.

Nov. 16. 2009 / 3:00PM, ADDXF.PK - ADDEX PHARMACEUTICALS LTD ADX10059-204 GERD Monotherapy Data

**Olav Zilian** - Helvea - Analyst

So it's too weak to make a read across for the migraine study?

**Charlotte Keyword** - Addex Pharmaceuticals - CMO

Yes. You can't really make a read across to the migraine study from that. Nice though it would be, I'm afraid we can't really.

**Olav Zilian** - Helvea - Analyst

And otherwise, would you have any other observations made that would be relevant for other indication? So I remember that this class of mGluR5 negative allosteric modulators would have the potential to be active in pain or anxiety potentially.

**Charlotte Keyword** - Addex Pharmaceuticals - CMO

Yes, we're looking at anxiety and depression sub-scores on this. Those data are still being analyzed at the moment and not in the top line results. So, we are looking at that. Again, it's quite a short term duration of treatment, two weeks, so you may not expect to see anything in two weeks of treatment, but we will look at that as part of that, and also in four-week study we're looking at that.

Talking about pain, what's even more interesting, we did see a significant impact on lower abdominal pain in the patient reported outcomes, a sub-score of low -- a subscale score of lower abdominal pain was significantly improved by the use of 10059. So, that's just a sort of point of interest.

**Olav Zilian** - Helvea - Analyst

Okay. Thank you very much.

**Operator**

(Operator Instructions)

We have a follow-up question from Mr. Peter Welford from Jefferies. Please go ahead, sir.

**Peter Welford** - Jefferies - Analyst

Sorry, just following off on the comment you just made about the pain and the anxiety. Surely if there's fewer reflux episodes, I mean the patients do experience less abdominal pain. So I guess how is it possible with both the anxiety and the pain to sort of disaggregate, I guess, or is it not possible, the effects of a drug versus the effect of having an effect on reflux, therefore obviously resulting in better pain and anxiety scores?

**Charlotte Keyword** - Addex Pharmaceuticals - CMO

Well, I think it's quite -- we're looking at the subscale that actually was positive was lower abdominal pain. But I mean, I think you're right, you've got an overall effect. In fact, you see -- talking of pain, again, you do see some impact on heartburn and heartburn severity as well, so that's obviously another type of pain that's going on.

Nov. 16. 2009 / 3:00PM, ADDXF.PK - ADDEX PHARMACEUTICALS LTD ADX10059-204 GERD Monotherapy Data

So looking across overall, there does seem to be some impact on pain. How you precisely tease it out in the context of this study is not clear at the moment. But I think overall the message is quite encouraging; there do appear to be impacts on some pain sub-scores in the study.

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**Peter Welford** - *Jefferies - Analyst*

Okay. That's great. Thank you.

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**Operator**

The next question is a follow-up question from Mr. Mike Aitkenhead from Piper Jaffray. Please go ahead, sir.

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**Mike Aitkenhead** - *Piper Jaffray - Analyst*

Hi. Thanks for taking my follow-up question. It just really is looking at the safety and tolerability again. Did you possibly have the data to hand on the rates of nausea, blurred vision and/or vomiting that was seen in the study? Because I do recall these were side effects that were also more predominant with ADX10059 in the Phase IIa study.

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**Charlotte Keyword** - *Addex Pharmaceuticals - CMO*

Yes, and they're very low. They haven't -- they're definitely under 5% because they're not on my summary that I have in front of me, so they are low. And unlike what we saw in the Phase IIa with that immediate release capsule where nausea and blurred vision were quite common, they were not common in this study at all.

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**Mike Aitkenhead** - *Piper Jaffray - Analyst*

Okay, that's brilliant. Thanks.

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**Operator**

(Operator Instructions)

Ladies and gentlemen, there are no more question from the telephone.

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**Vincent Mutel** - *Addex Pharmaceuticals - CEO*

Okay, thanks very much for your participation to this webinar. For sure there will be more information to be disclosed later on. We will publish these results and we'll present that. For sure as well we are now looking for the outcome of the 205, which has more dose groups, so it's going to be interesting to see what lower dose are doing in these -- on this type of indication as well.

Again, thanks very much for your attention.

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**Chris Maggos** - *Addex Pharmaceuticals - Head of IR and Corporate Communications*

Just a reminder, the presentation slides from today are available at the very bottom of the broadcast window for the webinar. They're hard to see, so you might miss them. And we'll post them on the website later. Thanks very much.

Nov. 16. 2009 / 3:00PM, ADDXF.PK - ADDEX PHARMACEUTICALS LTD ADX10059-204 GERD Monotherapy Data

**Vincent Mutel** - *Addex Pharmaceuticals* - CEO

Goodbye.

**Operator**

Ladies and gentlemen, the conference is now over. Thank you for choosing the conference call facility, and thank you for participating in the conference. You may now disconnect your lines. Goodbye.

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