

# FINAL TRANSCRIPT

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## **ADXN.S - ADDEX PHARMACEUTICALS SA and Merck & Co. Collaborate to Develop Drugs for Parkinson's Disease - Conference Call**

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## CORPORATE PARTICIPANTS

**Chris Maggos**

*Addex Pharmaceuticals - Head, IR & Communications*

**Vincent Mutel**

*Addex Pharmaceuticals - CEO*

**Tim Dyer**

*Addex Pharmaceuticals - CFO*

## CONFERENCE CALL PARTICIPANTS

**Philippa Gardner**

*Lehman Brothers - Analyst*

## PRESENTATION

**Operator**

Good morning and good afternoon. This is the Chorus Call conference operator. Welcome to the Addex Pharmaceuticals conference call. (Operator Instructions). At this time, I would like to turn the conference over to Chris Maggos, Head of IR and Communications of Addex Pharmaceuticals, accompanied by Vincent Mutel, Chief Executive Officer, and Tim Dyer, Chief Financial Officer. Please go ahead.

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**Chris Maggos - Addex Pharmaceuticals - Head, IR & Communications**

Thank you, Pascal, and good day, everyone. We are pleased to bring you the news of our deal with Merck & Co. Today, on this conference call and Webcast, Vincent Mutel, CEO of Addex, will describe the agreement with Merck. Tim Dyer, CFO, will describe the terms and update our financial guidance for 2007. Then Vincent will give some background on Parkinson's disease, the mechanism that Merck and Addex are targeting. And finally, before we open the call to your questions, Vincent will review the Addex partnering strategy.

Vincent?

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**Vincent Mutel - Addex Pharmaceuticals - CEO**

Thank you, Chris. Good morning, good afternoon, everyone. It is my real pleasure to announce the establishment of a partnership together with Merck to collaborate, to discover and develop positive allosteric modulators of one of the metabotropic glutamate receptors, which is the mGluR4.

This deal will be focused on the development of mGluR4 PAM, positive allosteric modulator, leads that have been discovered by Addex that we are going to move together with our partner up through the clinical candidate selection, and then at this stage, Merck will be responsible for moving the best molecule through the preclinical and the clinical development.

As you can see, we'll participate on the Addex side on two committees, the joint research committee and the joint development committee, which will have the mission to make sure that the most effective development will take place for our molecule.

The first indication to be pursued is Parkinson's disease. As we announced in our press release, we will develop molecules for additional indications. Unfortunately I am not able to disclose to you the nature of these indications today.

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And on this, I will give the floor to Tim who is going to tell you the financial terms of this deal.

**Tim Dyer** - *Addex Pharmaceuticals - CFO*

Thanks, Vincent, and good morning, good afternoon, everybody. So the financial terms, Addex will receive \$3 million in an upfront payment. We will also be eligible to receive \$106.5 million in research, development and regulatory milestones for the first product in multiple indications. Addex will also be eligible for an additional \$61 million in regulatory milestones for a second or third product, and we also will be eligible for undisclosed royalties on sales. Addex has also received an option to co-promote market products in undisclosed EU countries.

Now, moving on to the revised financial guidance for 2007, the revisions are primarily due to the upfront, which we are expecting to receive in cash in December. So the previous guidance given in July was operating cash burn of \$35 million to \$40 million and CapEx cash burn of \$3 million to \$4 million.

Now, the revised guidance has basically now been tightened up, and again, I reiterate we have taken account for this \$3 million which we are expecting to receive. So now it is CHF33 million to CHF34 million, and the CapEx has been revised slightly downward to CHF1.5 million to CHF2 million.

On that note, I hand back to Vincent.

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

Thank you, Tim. Let me drive you through the indication we are going to focus on with our partner, Merck. So we have developed or we will develop this molecule, our mGluR4 positive allosteric modulator, for the treatment of Parkinson's disease. As you know, Parkinson's disease is a long-term degenerative brain disorder, for which the cause is currently unknown. It is believed to be potentially coming from the overproduction of protein, which is leading to the loss of dopamine-producing cells in the areas of the brain which are involved in the control of movement.

The symptoms include tremors, rigidity and slowness. There is huge unmet medical need and a large market for the treatment of Parkinson's disease. As you know, 1.5 million patients currently have Parkinson's disease in the U.S., and about 60,000 new cases are diagnosed in the U.S. every year.

The current three marketed products are clearly helpful, but there is still significant room for improvement. We are not having a molecule on the market which is reducing dependence on L-DOPA. As you probably know, L-DOPA therapy is leading to tolerance and the development of side effects, which prevents its use for too long-term in the patient.

There is also no marketed product so far which works through a non-dopaminergic mechanism. Various companies have been developing new approaches, like the Adenosine 2A antagonist, but so far there is nothing which has reached the market successfully.

And finally, there are certainly no marketed products that can slow the disease progression, and in this regard it is quite interesting to focus on this new mechanism of action, which is the activation of the metabotropic glutamate receptor 4 for the treatment of this disease.

The reason why we have been following this approach at Addex and, very clearly at Merck, is because Merck has been pioneering the research in the mGluR4 activation. So they have very clearly shown that mGluR4 activation has efficacy in Parkinson's, which was largely identical to dopamine receptor stimulation. This has been shown by Merck researchers in several models of acute and chronic model of Parkinson's disease. Very interestingly, additional works by this team and others show that mGluR4 positive allosteric modulators, so not a direct agonist, could be as effective as mGluR4 direct agonist in this model.

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The mGluR4 activation is active through a non-dopaminergic system that is very interesting and important information in producing transmission at the connection or the pathways which are involved in to the disease. It has been demonstrated that in dopamine-depleted animals, the mGluR4 activation is still present. And that is very good, because we have, for the first time, access to medication which could be combined with the existing therapy, or which could play a role in dopamine sparing or L-DOPA sparing in these patients.

Additionally, other scientists from various places in the world have shown that mGluR4 receptor activation may have also a direct neuroprotective effect. The reason for that is that mGluR4 receptor is a post synaptic receptor and is working by decreasing the glutamate release and thereby is potentially able to reduce the neurotoxicity, which is associated to the glutamate over activation.

I think this is a very important step for our organization. Addex, as you know, has this expertise in allosteric modulation. We have established Addex as the one key leader in the allosteric modulation, and I think it is very important for us to stress that the partisanship established with Merck is another validation of competence in our leadership in this field.

So clearly, finding such molecules, mGluR4 positive allosteric modulators, has been a challenge for the industry. There are very few examples of such molecules which have been presented to the public domain. I think through this collaboration, Merck will have access to our selective molecules. We have a program which is in the lead optimization stage, and we are very happy and very proud to be effectively developing this molecule together with such a significant partner.

I should stress again that the strategies of Merck is not limited to the field in which they have been playing a pioneering role, but also in their competence for development of Parkinson's disease products, and we are extremely pleased by the way the partnership is established and potential for the development of our drug.

I would like to remind you that we signed in 2004 a similar deal around the mGluR2 positive allosteric modulator for the treatment of anxiety and schizophrenia with Ortho-McNeil, which is a Johnson & Johnson Company. We have today two of the most significant pharma companies in the world as partners and I think it is a significant achievement.

I will spend some time to give you again some precision on our allosteric modulator capability. We have the goal to be the world-class pharmaceutical company developing this type of molecule. And I will explain to you again a little bit about this technology that we have developed and that we are controlling and mastering here.

So essentially, we have molecules which are active on GPCRs and opposite to the classical approach, which has been to develop competitive ligands which are going to compete with the endogenous agonists for the site where they normally bind. We have developed molecules which are activating or blocking the receptor by binding at another site, which is present on the same GPCR, which is known as the allosteric modulator site.

You see here the effect of a negative allosteric modulator, which demonstrates that in presence of large quantity of the endogenous ligand, there is a significant reduction of the signal through the GPCR, and as you can see on the graph, our molecule is interacting with the part of the receptor which is not the one which is interacting with the endogenous ligand.

On the other hand, for positive allosteric modulators, you'll see the reverse effect, that in presence of smaller quantity of endogenous ligands, our allosteric modulators are able to increase the signal significantly, which is important because guaranteeing the physiology of the system where we will renormalize or normalize the system in case of pathophysiological conditions, and we will preserve the natural environment and function of the receptor.

This technology will allow us to identify molecules which have very interesting and differentiated properties compared to orthosteric or so-called competitive ligands. As you can see in the case of orthosteric, agonist and antagonists are activating and blocking the receptor at steady-state for a period of time, which are not fitting or not corresponding to the natural stimulants that you can observe on the value stimulation curve that you see on the screen.

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So, on the left-hand side, you see the agonist classical competitive ligands are increasing the response irrespective of the timing. And antagonists are blocking the response when not appropriate for the normal function of the receptor.

On the other hand, on the right-hand side, you see that allosteric modulators are effective when needed and only when needed. Negative allosteric modulators have given the property or the possibility to partially block the response, which is something which is not possible to achieve with classical competitive antagonists, and positive allosteric modulators at the right time are able to restore the normal function of the receptor, which might be affected in pathophysiological condition.

We are targeting, and that is on the next slide, all the families of GPCRs so far. We are not limited in terms of technology. We probably can address other family of targets besides the GPCR family. But very clearly, in orange, you can see the receptor on which we have been active, or publicly disclosed activity so far. The GLP1 receptor is one in the family two. In the family three, we have pursued development of several mGlu receptors, and today we are also very -- I think it is very important to recognize that we have disclosed for the first time that we have been working on the mGluR4 receptor as well. We have a program with GABAB and we have a program in family one on the FSH receptor, which has been quite successful so far.

This is leading me now to disclose or to discuss together with you the pipeline on allosteric modulators that we have and our partnering strategy. As you know, ADX10059 is our most advanced clinical candidate. It is a mGluR5 negative allosteric modulator coming from our technology. We have been able to demonstrate the activity of this molecule in very large indications, like GERD and migraine. This has very interesting potential for the future. We are still conducting the acute anxiety trial, for which we will announce the results of the end of this year, beginning of next year.

Our partnership strategy for this molecule is to enter into partnering only after Phase IIb in GERD study, at least. We are still discussing very heavily the potential of this product with our investigators and very clearly as well with potential pharma partners. It is a very important part of our strategy. We are gathering all the information about how to maximize the potential success and development of this molecule.

The second compound, which is also available for partnership, is ADX63365. This is a mGluR5 positive allosteric modulator. It has an extremely interesting mechanism of action potentially for the treatment of schizophrenia and cognitive impairment. There's a lot of effort in the pharma today around this mechanism of action, and the results are extremely encouraging. We are actively looking for a partner for this program, and I hope that we will be able to come with some news on that at one point of our development.

Regarding the development of our GABAB positive allosteric modulator, ADX71441, we intend to move this project all the way through to registration for spasticity at least. It is an interesting new mechanism of action as well. There are potential for development besides spasticity for GERD and anxiety and potentially other indications like urinary incontinence, and we will certainly take this into account in our clinical development.

We have a very interesting molecule coming from the FSH negative allosteric modulator program, ADX68693. This compound has been developed for the treatment of osteoporosis and also in contraception. We are very interested to follow the osteoporosis path for development and will consider certainly partnership following the proof of concept that we are currently developing in vivo in animals, and we plan to start the molecule in Phase I at the beginning of 2009.

You know now that we have an mGluR4 PAM program for Parkinson's disease, and we are very happy to have signed this deal with Merck, having now the right expertise and muscle beside us to be able to make this program a very big success.

And I will close on GLP1 positive allosteric modulator program, which is being developed for the Type II diabetes. It is a small molecule, potentially orally active, and very clearly we will not partner that before the end of the Phase IIb, when we will have maximized the return on such a program.

With this conclusion on our clinical pipeline, I will now -- we will now take questions from the participants. Thank you.

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## QUESTIONS AND ANSWERS

### Operator

(Operator Instructions). Philippa Gardner, Lehman Brothers.

### Philippa Gardner - Lehman Brothers - Analyst

I just wanted to dig a little deeper into the financials, and I appreciate that you probably won't be able to answer half the questions that I have, but I will ask them anyway.

First of all, just on the milestone payments, am I right in assuming that you're not getting any sales-related milestone payment? It is all just to do with development and regulatory milestones?

And then secondly, on the royalties, can you give us some kind of sense are these flat royalties or step royalties? Are we looking at sort of high single digit or just some kind of clarification there?

And then, I was just wondering if you could kind of talk me through what the next steps are with this plan and when we might see this compound in the clinic? Thank you.

### Tim Dyer - Addex Pharmaceuticals - CFO

I will take the first two. So yes, the milestones are research, development and regulatory, and there are no sales milestones. The royalties, we can give you no guidance on those.

And for the third question, I will hand that back to Vincent.

### Vincent Mutel - Addex Pharmaceuticals - CEO

We are at a very early stage. I think, that is an interesting part of the equation because we have a program which is in early lead optimization. As a perspective about if it will be difficult to do, in particular in this indication where you need a lot of confirmation in any more particular about the potential of the drugs, this is a new mechanism of action, and we will certainly leave our partner to decide on the best possible way to move this program forward, knowing that you can see a lot of potential combinations for the development.

So I cannot really be more precise on the timelines for reaching the market for such a product. But I can tell you that because it is a new mechanism of action, there will be certainly a lot of interesting experiments to be done both in animal and man.

### Philippa Gardner - Lehman Brothers - Analyst

And if I can just have one very quick question on 59, can I just ask how the formulation for that is progressing?

### Vincent Mutel - Addex Pharmaceuticals - CEO

The formulation with 59 is an important aspect of the development of the drug. As you know, we have been through already optimization of this formulation. We are currently conducting the PK study in dogs to assess the new formulation that we have

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developed. And on the back of that, we will select one formulation to go to Phase I. Currently, we are on time and on track with the development of the formulation of 59.

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**Operator**

(Operator Instructions).

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**Chris Maggos** - *Addex Pharmaceuticals - Head, IR & Communications*

If I may, maybe, Vincent, you would like to discuss or differentiate the mechanism of 63365 with the mGluR2 PAM?

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

Indeed, that is a good point. The mGluR5 positive allosteric modulators are mostly drugs which have been seen as a potential treatment for cognitive decline. The results, which are coming from the animal experiments, point out to what direction the mGluR2 positive allosteric modulator or mGluR2 agonist that have been developed by Lilly have not shown or have not displayed so far any indication of efficacy for cognitive disorder or cognitive declines.

So they are going to be potentially used for the more positive symptoms and potentially some of the negative symptoms as was shown by Lilly, but we do not believe that it might be useful for the treatment of the cognitive decline.

So there is a real interesting complementarity of the mGluR5 PAM compared to the mGluR2 PAM, and we believe that both type of molecules will have future in development in at least schizophrenia and potentially for mGluR5 PAM in cognitive disorder associated with Alzheimer's disease or even Parkinson's disease where there is a cognitive decline taking place.

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**Operator**

Philippa Gardner, Lehman Brothers.

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**Philippa Gardner** - *Lehman Brothers - Analyst*

I seem to have the floor to myself, so I'll take this opportunity to ask as many questions as I can. Can I just ask probably Vincent what you think the next product that you will partner might be?

And then also, just a question for Tim as well. So obviously this year we are getting the \$3 million upfront. What do you think you might get in revenues next year I guess it's kind of a rephrasing of the question I asked earlier about what the next stages are for the development of this collaboration?

That would be really helpful. Thank you.

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

I think also we cannot give precise timelines for dealmaking. As you know, it is an activity which is always depending not only on one single part of the partnership. We can tell you and I think we have been clear for the mGluR4, at least, we disclosed that we have been proactively looking for a partner for this program for already some time. This is the same for 63365, for which we have activity, and we are actively looking for a partner.

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So if I can predict some things, certainly we have put quite a lot of time into 63365 discussions with partners. I think that 59 is an interesting case. We clearly want to move the product forward up to Phase IIb and post-Phase IIb for the partnership. But, as I said before, we have taken care to discuss with large pharma organizations to make sure that our development is not going to jeopardize the Phase III. So this has created some interesting friendships. And we have, as you can believe, been discussing with very, very good organizations.

So this is I think the two major things on which we can draw your attention. 63365, as we always said, we are looking for partners for this program.

On the second question, I think Tim is going to answer.

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**Tim Dyer** - *Addex Pharmaceuticals - CFO*

The figure that I gave you, the \$3 million upfront, we are expecting to receive the cash for that in December. Clearly, that is an upfront. Under the accounting rules, we are required to amortize that over the two years of the research phase. So with the effective date of the collaboration being November 30, you can expect to receive 1/24 of that number in 2007 revenue line. The rest will be recognized on a monthly basis going forward for two years.

Now, we don't speculate about the receipt of any of the milestones going forward.

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**Operator**

Gentleman, there are no more questions at this time.

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**Chris Maggos** - *Addex Pharmaceuticals - Head, IR & Communications*

Well, thank you all very much for joining us today. We were very pleased to have some good news for you, and we look forward to talking to you again as we visit your various locations and in our next conference call.

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

Thank you very much.

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**Operator**

Ladies and gentlemen, the conference has now concluded, and you may disconnect your telephone. Thank you for joining and have a pleasant day. Goodbye.

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