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Start of Transcript

Operator: Thank you everyone for standing by. Welcome to the Actinogen Medical Advisory Board Investor Conference Call. At this time all participants are in a listen only mode. I am joined today by Actinogen Medical's CEO Dr Bill Ketelbey and Advisory Board members Chairman Professor Craig Ritchie, Professor Colin Masters and Dr Jeffrey Cummings.

There will be a short introduction by Dr Ketelbey followed by a question and answer session at which time if you do wish to register a question please press the star key followed by the number one on your telephone keypad. Please be advised that this conference is being recorded today 14 April 2015. I would now like to hand the conference over to your first speaker today Dr Bill Ketelbey. Go ahead, thank you.

Bill Ketelbey: Thanks very much and good morning to all of you. I'm delighted to be joined today by our recently appointed Xanamem Clinical Advisory Board. As you heard Professor Craig Ritchie who comes to us from Edinburgh University, Professor Colin Masters down at Melbourne University and Professor Jeffrey Cummings at the Cleveland Clinic in the USA. I'd like to pay particular attention to and thank both Craig and Jeff for being on the call. Jeff who is in the USA, it's now early evening and he's joining us from the USA. He does have another commitment so will only be with us for about half of the call unfortunately.

Craig Ritchie who joins us from Edinburgh, it's now midnight over there. So a particular note of thanks to Craig and Jeff for joining us on this conference call. The appointment of these three world leading experts in Alzheimer's and prodromal Alzheimer's disease to our Advisory Board has been a particular - particularly noteworthy for Actinogen Medical. Given that all these three members bring such significant global experience in Alzheimer's disease research, their collective experience and expertise and intellect will help position Xanamem clinical research at the forefront of the diagnosis and treatment of early and prodromal Alzheimer's disease.

As we've announce previously the Advisory Board's first task is to assist Actinogen in designing the optimum place to trial - to best demonstrate the efficacy and safety of Xanamem which is our lead compound in Alzheimer's research in patients with Alzheimer's disease and mild cognitive impairment or a disease that's probably better termed prodromal Alzheimer's disease now. I am pleased to say that we have received the Advisory Board's sign off for the outline of our Phase II trial already.

We held the first meeting of the Advisory Board some three weeks ago and have received the sign off of the outline of the Phase II trial. This will - this outline will be further developed over the next few months leading to us beginning the Phase II trial in patients with Alzheimer's and prodromal Alzheimer's disease in early 2016. I'm extremely proud that Actinogen has this level of expertise at hand and I'm also hugely impressed by the Board's commitment and passion for our goal of developing Xanamem as a promising new treatment for Alzheimer's disease.

I'll now hand over to the gentlemen for the people to ask questions of the Advisory Board. But as a lead in to the questions perhaps I'd just open up with a question to each of the Advisory Board members and ask them each if they could perhaps give a short comment on their background in Alzheimer's research and then a quick comment on what drew them to join the Xanamem Clinical Advisory Board? What attracted them to the Board? So perhaps if we could start with the Chairman Professor Craig Ritchie in Edinburgh, Craig.

Craig Ritchie: Thank you very much Bill, thanks for that welcome and introduction. So I actually started in the Alzheimer's space way back in 1997 when I worked with Colin in the Mental Health Research Institute in Victoria. That really opened my eyes and set the scene for what has now been - gosh almost 20 years now of working in this area. Six months ago I moved from Imperial College London to the University of Edinburgh to a chair there in Psychiatry of Ageing.

I guess the main interests I have in Alzheimer's disease are (1) around the epidemiology particularly in mid-life and prodromal disease. But married to that obviously a strong link into interventional studies particularly psychopharmacological studies and with the target Xanamem is looking to hit in terms of Alzheimer's pathology and symptoms that are generated therein. That in itself was a huge carrot if you like for me to want to be part of the development of this asset moving forward.

I think also the other key thing for me was this target, this willingness and the wish really to make a big difference to patients who have Alzheimer's dementia. There's a huge amount of work obviously going on in the disease modifying space but I think where we start with Xanamem to try and improve symptoms of people with mild early dementia is particularly noteworthy and I'm very much attracted to the - as a working frontline clinician as well as an academic.

Bill Ketelbey: Thanks very much Craig. Jeff perhaps if we could get a quick comment from you.

Jeffrey Cummings: Sure, Jeff Cummings, I'm a Professor of Neurology in the Cleveland Clinic. I'm responsible for the Alzheimer's disease programs across the Cleveland Clinic including in Cleveland Ohio, Las Vegas Nevada and Western Florida. I've been also involved as Craig has for a long period of time in Alzheimer's disease clinical trials and been very interested in therapeutic development. I was the Director of the Alzheimer's Disease Centre at UCLA for about 20 years before I came to the Cleveland Clinic about five years ago.

What attracted me to the development program of UE2343 is that - now we've working primarily with Alzheimer's disease compounds and although there is interest in these compounds and continuing promise I think it's clear that we need to expand the repertoire of mechanisms that we're looking at and the way we're thinking about therapeutic interventions in Alzheimer's disease. The idea of looking at non-amyloid related interventions is a very welcome avenue of therapeutic exploration and I thought this was one of the most interesting compounds I'd seen.

Bill Ketelbey: Thanks Jeff and Colin a comment from you.

Colin Masters: Thanks very much Bill. It's a great pleasure to be with you on this exploratory journey to see if lowering cortisol levels in the brain will have a beneficial effect. Like Jeff has just said these non-amyloid approaches deserve to be explored. We're in a situation at the moment where we don't have an effective

therapy for the cognitive impairment particularly in prodromal phases of Alzheimer's disease. So I've spent the better part of my research career looking at Alzheimer's disease and trying to understand the mechanisms that drive it relentlessly forward.

We discovered the amyloid protein structure back in the 1980s and we've been working on the amyloid protein ever since. There's a lot of optimism in the field at the moment that some form of treatment will eventuate and I want to do everything possible to speed up this process. So I think that Xanamem has the potential to provide this cognitive benefit that we're seeking and I look forward to working with you and the other Board members to test whether this idea is going to work or not.

Bill Ketelbey: Thanks Colin and thanks to all three of you. I'll hand back to the meeting facilitator now to continue with the investor call.

Operator: Thank you very much. At this time if you do wish to register a question please press the star key then one on your telephone and wait for your name to be announced. If you wish to cancel your request please press the star key then two. We will just pause for a moment to allow questioners to enter the queue. Thank you, today's first question is from Shane Storey from Wilson HTM, go ahead, thank you.

Shane Storey: (Wilson HTM, Analyst) Hello, can you hear me?

Bill Ketelbey: Yes.

Shane Storey: (Wilson HTM, Analyst) Good morning or evening depending on where you live. But look I wondered if you could begin for me by explaining - well the intriguing thing for this fund is where cortisol fits into the aetiology if you like of mild cognitive impairment and potentially Alzheimer's. I mean certainly you know see, get and understand the elevated cortisol and how that worsens the condition but how much is known about how that starts to occur and where the right point of intervention might be?

Craig Ritchie: So shall I kick off.

Shane Storey: (Wilson HTM, Analyst) Sorry, yes, it's a tough question, big question, long question.

Craig Ritchie: Well I mean I can maybe start off. I'm sure Colin and Jeff will have something to add to this, Craig here. I mean I think for a very long time and I think you alluded to this there's been an epidemiological association between what we euphemistically described as stress and a variety of different neurodegenerative conditions, not least a very strong association from both prospective and retrospective studies of depression with - being a very significant risk factor for the development of Alzheimer's dementia.

I think what underpins a lot of those associations from a biological basis is disturbance with the HPA axis. So drilling down to look what the biology of that interaction if you like between HPA axis to function and neurodegenerative disease, what we have found through numerous studies both in man and more particularly in animals is the incredible sensitivity of the hippocampal, hippocampal structures which of course are critical in Alzheimer's disease or felt to be critical in the pathology of Alzheimer's disease and the genus symptoms.

It would seem that elevated cortisol levels do seem to have an effect on neurotransmission and the hippocampal structure itself. So I think that was the basic observations, or [unclear] of observations that led

to many groups actually looking to intervene in that process to see whether or not inhibition of HSD could actually have a beneficial effect over time. Now before I pass onto the others I think you highlighted a very important point and when is the critical window when it may be of use to dampen down this response? Is it in mid-life or is it in people who already have symptoms?

I think what's of interest is that there have been studies both in animals and man which suggested that even in people with maybe normal ageing or early symptoms there has been an effect on HSD inhibition in improving cognitive function. So I think that gave us a great deal of optimism that a specific targeting of this enzyme would be of benefit to people with Alzheimer's dementia.

Shane Storey: (Wilson HTM, Analyst): I guess a follow up is - thank you for that but look a follow up would be - I mean - and pardon if this sounds like I don't know enough but I mean is HSD1 - I mean is it the only channel I guess through which you can have elevated cortisol? Is it the only way it sort of comes to that? I guess the question really reads into the validation or otherwise of the target. Is the - I guess what's the best evidence we have that this enzyme is the right target for that objective?

Jeffrey Cummings: Well I'll take part of that. HSD1 is a critical enzyme in the glucocorticoid system and I think it remains to be proven comprehensively that inhibiting the enzyme will do what we want it to do. But the pre-clinical work is compelling and the - as Craig said the distribution of the receptors is such that it looks to the phenomenology of Alzheimer's disease. So we have the receptor profile, we have enough information about the activity of the enzyme to believe that the enzyme inhibitor should have a critical role in decreasing the glucocorticoid exposure.

I think so far the work in normal volunteers looks like we can do this safely and the critical question will be in the Phase II trial to show that we have a symptomatic benefit in patients with Alzheimer's disease. I think the pieces are in place from the genetics, the pre-clinical observations and the clinical observations so far to make us optimistic about the program.

Colin Masters: So it's Colin here, Colin Masters. If I could just add to what's been said by Craig and Jeff that there is emerging evidence and quite convincing evidence that elevated cortisol levels particularly in the cerebrospinal fluid are an indicator of the rate of progression of cognitive impairment particularly in the prodromal phases. So that gives us a lot of confidence that this will be a valid target for ameliorating that rate of change.

Shane Storey: (Wilson HTM, Analyst): Thank you and look my last one is - so the objectives then would be - just checking if this is right looking ahead to the Phase II study, so you'd be wanting to achieve a complete blockade of the enzyme in the brain, is that right?

Colin Masters: Lowering the levels to normality would be an appropriate target.

Shane Storey: (Wilson HTM, Analyst): Okay, that's it from me, thanks gentlemen.

Operator: Thank you, the next question is from David Langsam from *Biotech Daily*, go ahead, thank you.

David Langsam: (*Biotech Daily*, Journalist) Good morning, good afternoon and good night to Craig Ritchie. I've got to say that one of the reasons for the question is of course that I'm just a sucker for a Scottish accent

as we all are down here. Two questions and I guess the first one is on trial design. Colin will be exceedingly aware of the recent PBT2 results from Prana of which he's an advisor and there was - and given that you're not going for amyloid plaque therefore an imaging process is not going to be part of the determination of efficacy. There's a great concern over the cognitive tests that they're very subjective so I'd like to know how you're going to measure efficacy in this particular trial? So that's the first question.

The second question goes to the use of UE2343 and evidence for it. As I understand you're saying that the cortisol appears to be the problem but cortisol has been - particularly in this - as I - and again my knowledge of medicine is very, very sketchy. But as - from what - everything I've read it seems to have some effect and has been designed for stress and metabolic syndrome and the only evidence that I've seen - and I'm very happy to receive any papers that you'd like to send me on UE2343 or Xanamem for Alzheimer's - is apparently a 20 year old rat test that showed that lowering cortisol was useful and that increased levels of cortisol increased lesions.

Is there any further better evidence of the link between UE2343 and a reduction of Alzheimer's disease? So I'll rephrase the two questions. How are you going to measure efficacy and is there any robust evidence that UE2343 or Xanamem has any efficacy for Alzheimer's disease?

[Craig Ritchie]: [Maybe I can take the call]...

David Langsam: (*Biotech Daily*, Journalist) Like I said I'd like [unclear] to go through Craig.

Craig Ritchie: Okay, well despite - I didn't lose my Scottish accent working for four years in Melbourne, Australia obviously and living in London for the 20 years. I'm also involved with - like Colin and Jeff actually with the Prana program both on the - all of us on [unclear] of that but we're all aware of what's been published in that area. I think the first question is a very important one and it's how we're going to measure clinical efficacy.

I think when we decided when we met in Nice at the first Advisory Board that the target population for this would be a group who have mild symptomology but still within the dementia range rather than going into an area of prodromal or pre-clinical population and there are several reasons for that. But not least because over a 12 week period one would expect some degree of decline in people who have got mild dementia as opposed to the stability one often sees in people with MCI over a period.

So we had some discussion and I'll pass to Jeff in a moment about what the best outcome measure would be for that particular population. One we rested upon was something called the ADCOMS and I'm going to let Jeff talk to that more than I can because he's much more experienced with it than I. But it's basically an amalgamation of the better moving parts of the MMSE, the ADAS-cog and the CDR some of the [boxes] because it's the drugs if you like opportunity to show an effect over a 12 week period.

David Langsam: (*Biotech Daily*, Journalist) These are cognitive tests?

Craig Ritchie: They're all cognitive tests, yes, absolutely. I think really at this stage we would be most keen to see a cognitive readout rather than necessarily a - say for instance a biomarker readout because there isn't if you like a strong biomarker that we could actually be targeting.

David Langsam: (*Biotech Daily*, Journalist) So with the short 12 week medication program you'd have to have a lot of patients randomised to be able to see a difference, a significant difference. Have you done the maths on how many would be required?

Craig Ritchie: Well we're working on the premise it'll be around about the 200 mark.

David Langsam: (*Biotech Daily*, Journalist) About 200 patients in the Phase II trial.

Craig Ritchie: Yes, correct.

David Langsam: (*Biotech Daily*, Journalist) Excellent.

Craig Ritchie: Jeff do you want to say more about the ADCOMS?

Jeffrey Cummings: The ADCOMS.

Craig Ritchie: Yes.

Jeffrey Cummings: Let me pick up the ADCOMS discussion. This is something that's been advanced by the CAMD, the Coalition Against Major Diseases which is part of the FDA's Critical Path Institute and what they're charged with is developing instruments that better tell us the effects of drugs or report out on drug/placebo differences. So we have done a very extensive analysis of the portions of existing tools that move either with change and disease in the placebo group or in response to treatment with a cholinesterase inhibitor which are the available agents where we can look at a therapeutic response.

Across a wide of instruments there were four elements within the ADAS-cog, two elements within the mini mental state and all elements of the CDR that moved well in concert and produced the greatest signal to noise ratio in the placebo group or in the treatment group respectively so that…

David Langsam: (*Biotech Daily*, Journalist) Jeff could you just run through those acronyms and translate them into…

Jeffrey Cummings: Yes, sorry. So the ADAS-cog is the Alzheimer's disease assessment scale cognitive portion. It's the standard outcome of the - of an Alzheimer's disease clinical trial. All of the existing agents that have been approved use that instrument. Then the MMSE is the mini mental state examination so a commonly used cognitive assessment, global cognitive assessment. Then the CDR is the clinical dementia rating. It has cognitive elements and it has functional elements so it is portions of those three tools that are very familiar to clinical trialists. So no new training will be required because this is not a new tool. This is a new analytic approach to be used as an outcome.

David Langsam: (*Biotech Daily*, Journalist) So the Alzheimer's disease, cognitive disease - sorry, could you run through the first one? Alzheimer's disease, cognitive…

Jeffrey Cummings: Yes, the Alzheimer's disease cognitive assessment, The Alzheimer's disease assessment scale, ADAS, Alzheimer's disease assessment scale, cognitive portion, ADAS-cog.

David Langsam: (*Biotech Daily*, Journalist) Right and then the mental state.

Jeffrey Cummings: Mini mental state examination and the clinical dementia rating.

David Langsam: (*Biotech Daily*, Journalist) Right.

Jeffrey Cummings: We've submitted a number of abstracts on this and it's currently before the FDA. As a matter of fact our meeting is in two weeks with the FDA to take the next step in the qualification process for having outcomes approved, an outcome for both Phase II and more importantly Phase III clinical trials. So we think that this is a very strong approach to begin using in clinical trials of Alzheimer's disease patients particularly where you're dealing either with prodromal disease or in mild dementia. We are not sure exactly how this analytic approach might work in either moderate or severe disease.

David Langsam: (*Biotech Daily*, Journalist) My last part on this first question is, so there can only be cognitive tests, there's no other way of measuring actual brain changes?

Jeffrey Cummings: It would be…

Craig Ritchie: Not over 12 weeks.

Craig Ritchie: A little bit over.

Jeffrey Cummings: Exactly, over 12 weeks it's extremely difficult to show something like changes in spinal fluid or changes in brain volume that might be meaningful. I'll let Craig and Colin comment on that.

Colin Masters: Yes, I think any of the biomarkers that we currently accept of Alzheimer's disease we're looking at change over 12 or 24 months.

David Langsam: (*Biotech Daily*, Journalist) Right and for evidence of UE2343 and Alzheimer's disease, is there anything other than the 20 year old US rat study?

Craig Ritchie: Yes, I mean I think - I don't know Bill if the [data] has been published yet but there's been - the work done in University of Edinburgh with this compound in a variety of animal models including transgenic Alzheimer's mice, have shown improvements in spatial memory testing which is done using a [wide] maze. There has also been - that was an aged rodent but there's also some work done in transgenic mice as well. So I'm not sure what of that is in the public domain but there has been work, some animal work leading up to these clinical studies.

Bill Ketelbey: It's Bill here. Yes, I'll comment. No, it hasn't been published. It's certainly much more recent than 20 years and it's all part of the drug development program put in place by the University of Edinburgh team over the last seven years that they've been developing Xanamem. So the data is available and it is direct evidence with the rodent models and will form - is forming part of the data set that is submitted to regulatory authorities and ethics committees when evaluating the trials that we're undertaking.

David Langsam: (*Biotech Daily*, Journalist) Bill are you able to get that data and publish the data? Not as a journal article but at least for you Company. Is the University of Edinburgh providing that?

Bill Ketelbey: Yes, oh, absolutely we have all the data available and some of it we have made available. It hasn't been published but I'll certainly get whatever evidence that is publicly available - I'll certainly get to you David.

David Langsam: (*Biotech Daily*, Journalist) I certainly wish all of you the very best for what sounds like an extremely exciting project particularly in the light of the inability of just about everyone else in the world to do anything on an unmet medical need, so thank you very much for answering my questions.

Operator: Thank you, the next question is from Michael Sistenich from Bell Potter Securities, go ahead, thank you.

Michael Sistenich: (Bell Potter Securities, Analyst) Hello, hi everybody. Thank you very much for having this call and taking my questions today. I have a few so I'll just do them one at a time. With regards to the ADCOMS and the way this is used in the various elements that have been picked out of the ADAS-cog et cetera is this something that you are using to identify in this Phase II trial as a particular signal for your [unclear] or is the expectation going to be that this is also going to be an acceptable end point, regulatory end point for the agency?

Jeffrey Cummings: I think this will - our goal through the institute is to make this acceptable to the agency. So the FDA has defined a qualification process and we have entered that. Now that doesn't mean that they're necessarily going to accept it. But this is the goal and CAMD is an offshoot of the FDA so they have a sort of inside track on developing tools that would be approved by the FDA and that it has entered the formal qualification process. The first two meetings with the FDA have occurred and we're hoping that it would be a regulatory end point.

Now we would not use it if it were - if it is not approved or if there is some question about it being approved for - as a regulatory end point. Then we would need to go back to a cognitive and functional end point in the traditional way.

Michael Sistenich: (Bell Potter Securities, Analyst) Okay, fantastic, thank you. I think Colin mentioned earlier on that cortisol levels in the CSF are indicative of rate of decline and I was just - I think that kind of raises an interesting question and there are two questions here. (1) is do you have the impact on cortisol levels that you would expect this product to have and secondly whether that translates into a clinical effect on your outcome? So my question would be, will you be looking at cortisol levels in the CSF as either an enrolment criteria or doing - I know it's going to be difficult but doing serials on that in order to demonstrate that you're actually having an effect on cortisol in the CSF during this Phase II trial?

Colin Masters: It's a good question. I think we've decided initially to just go with plasma levels to see how they respond in this Phase II study but obviously if it goes forward, if we see efficacy then in a future study I think we'd obviously like to be able to assure ourselves that the CSF levels are behaving in the same fashion as the plasma levels.

Michael Sistenich: (Bell Potter Securities, Analyst) Sorry, yeah, carry on, sorry.

Bill Ketelbey: It's Bill here. I just would make a comment. The trial obviously - the plan that we have is barely three weeks old and it's still got eight months of development ahead of it and questions like this are going to be re-evaluated and re-debated extensively over the eight months of development. So it may well be that this is a - one of the end points we do build into the study. So I would say it's difficult to answer a lot of the detailed questions because we're just not at that point in time with the protocol.

Michael Sistenich: (Bell Potter Securities, Analyst) Okay, fantastic, thank you Bill. Just one follow-up to that question, do we have an idea - are plasma levels of cortisol well correlated with CSF levels of cortisol, do we know that?

Jeffrey Cummings: Bill can you help with that or…

Bill Ketelbey: Well yes, the answer is yes. I'm just wondering if Craig wants to comment at all. The - work has been done quite extensively by the Edinburgh Team that developed Xanamem and a lot has been published on cortisol levels both CSF and plasma.

Craig Ritchie: Yes, no, no, I think that's right and I think there is obviously a correlation. I couldn't give you the actual sort of coefficient if you like but there is a reasonably tight correlation between the two. I think one of the more critical correlations to try and understand would be the relationship between CSF cortisol levels and what's actually happening if you like in the hippocampus and that's a much greater challenge.

Michael Sistenich: (Bell Potter Securities, Analyst) Yes.

Craig Ritchie: There have been some attempts at the University of Edinburgh to actually try and characterise that by looking at cortisol sampling from the internal - the external jugular vein in and out [unclear] et cetera and this is proving problematic. But what I would say and building on what Colin said ideally we would want to take CSF samples on everybody from this study because I think we need to explain a lot more as you do in a Phase II trial about mechanisms and prove concepts et cetera. The challenge of course is that with a study of this size if you were to insist upon CSF sampling you do have a major impact on recruitment.

Michael Sistenich: (Bell Potter Securities, Analyst) Yes, yes.

Craig Ritchie: So it makes almost an undoable study. So I think what we're planning to do is have it as an option for those who are willing to participate in a CSF sub study and then we'll explore in some detail just those very questions that you're posing about the relationship between plasma levels, cortisol and CSF levels.

Michael Sistenich: (Bell Potter Securities, Analyst) Fantastic, thank you. Then my final question here was really with regards to how rapidly Xanamem - you know your expectations that Xanamem is going to be able to affect the cortisol levels and where I'm going with this question is trying to figure out - cortisol levels affect many systems within the body and effects on mood and a number of other systems. So my question here is do we have an understanding of what base line levels and how rapid changes in cortisol may result in effects on mood, anxiety, cardiovascular effects et cetera?

Craig Ritchie: Yes, well if you think about our physiological response to heightened cortisol it's almost instantaneous thank goodness because it's what we need to maintain alertness and be able to respond to stressful events. So I mean the whole system is exceptionally dynamic and of course if one is specifically dampening down that cortisol response centrally then one would expect cognition could improve really quite quickly. But of course we're not looking to modify the normal if you like stress response. What we're looking to do is try and sort of just move it all down a notch over a longer time period with the HSD inhibition.

One of the things we're actually very purposely looking for is a safety signal to see whether or not you do actually induce depression, apathy symptoms that may be associated with low cortisol levels, [unclear] to date there's been so suggestion in Phase I studies of any of that actually taking place but we will of course be vigilant for that.

Michael Sistenich: (Bell Potter Securities, Analyst) Okay.

Bill Ketelbey: Perhaps maybe - it's Bill here - maybe I can just provide a little bit more information that might answer your question. We've got animal data - direct animal data and indirect human data that would indicate within six weeks we will certainly get a very adequate clinical response around the cortisol response. So our plan is to treat for 12 weeks and so we certainly expect within the trial time period to achieve a very adequate clinical response if there is one.

Michael Sistenich: (Bell Potter Securities, Analyst) Fantastic, thank you Bill, that does answer it because part of my question is about the rate of change where you rapidly start to adjust the levels of cortisol.

Bill Ketelbey: Yes, no, no, we have direct pre-clinical data that shows that the effect is achieved well within six weeks.

Michael Sistenich: (Bell Potter Securities, Analyst): Fantastic, thank you very much everybody for taking my questions.

Operator: Thank you, the next question is from [Andrew Foote from Aberdeen], go ahead, thank you.

[Andrew Foote: (Aberdeen, Analyst)] Hi guys and thanks for taking my question. My questions was just around this reduction in cortisol and whether or not that may be associated with other diseases or other indications which perhaps this drug could help with.

Craig Ritchie: Yes, that's a really good question. I mean drugs like carbenoxolone for instance have been looked at in people with type 2 diabetes. So there is potential that this could actually be used not just as a treatment for Alzheimer's dementia but maybe more specifically for people who have type 2 diabetes who are as everyone knows are at significant risk of developing cognitive impairment and then on top [primary] dementia. So I think there's a whole series of conditions which we'd be looking at, secondary indications with this particular approach.

[Andrew Foote: (Aberdeen, Analyst)] Do you think there's any chance that you can incorporate that into your clinical trials in the early stages?

Bill Ketelbey: Perhaps - it's Bill here - maybe I could comment on that. Clearly our primary target is Alzheimer's disease and the Advisory Board is tasked with ensuring we put together a protocol to define the efficacy and safety in Alzheimer's disease. But we have had a number of approaches and interests shown in our drug in areas as diverse as PTSD, in diabetes as Craig has indicated, perhaps even cognitive impairment in diabetes, in post myocardial infarction.

There are a number of areas both central nervous system indications like the present schizophrenia PTSD and metabolic indications like diabetes, cardiovascular disease, obesity. There are a number of potential indications that we could pursue. Our primary goal is obviously Alzheimer's but peripherally we certainly are

looking to how we are going to be able to concurrently also run studies in these other indications at some time in the future.

[Andrew Foote: (Aberdeen, Analyst)] Fantastic to hear and best of luck.

Bill Ketelbey: Thank you.

Operator: Thank you, the next question is from [Harif Mottay, private investor], go ahead, thank you.

Harif Mottay: (Shareholder) I think that's me. Good morning my name is Harif Mottay, I'm a shareholder. First of all thank you very much for doing this work. My father had Alzheimer's. I wanted to ask some few simple questions. They may have already been answered but I was hoping you could give them - give the answers in very simple terms because I don't have a medical background. What - have you established any side effects in your studies so far or will you do that at later stage? Could you also tell me if this drug will - can help any type of Alzheimer's disease? My father had a particular Alzheimer's disease where he was very clear one moment and the next moment he wasn't. I think it had to do with the blood flow to the brain and I was wondering if your drug is also targeting that. Thank you.

Bill Ketelbey: It's Bill here. Let me deal with the first question because that really relates to the Phase I studies that we have ongoing at the moment. The only human studies that we've done with our drug with Xanamem at the moment are Phase I studies, one done in the UK and one that we're currently running in Perth. I have to say that the safety profile from these two studies is exactly as we expected. No side effects, no untoward side effects that we - that concern us.

So the safety seems to be exactly as expected. No safety concerns or signals with this compound at all. But obviously as the trials evolve over time safety is one of the key outcome measures that we constantly evaluate so that we build the safety profile of the drug. But there's no reason to believe on the evidence that we have at the moment that there's any safety signal or problem with our compound. I might hand over to the Advisory Board to comment on the second question then.

Craig Ritchie: Yes, well I'm happy to pick this up Harif and sorry to hear about your father's condition. But I think it's often the case that we tend to describe people with Alzheimer's dementia or vascular dementia or Lewy Body dementia and all these various sub types, if you like, of dementia. I think what we're beginning to realise is that individuals don't really fit very neatly into these boxes in terms of a diagnosis and many people have different pathologies or different processes leading to a single sort of clinical presentation.

One of the critical overlaps is - with regard to blood flow to the brain is called cerebral vascular disease and it sounds from what you're saying about your father that it may have been that he had a small stroke or something and that was maybe to do with the blood flow to his brain rather than a more chronic sort of Alzheimer's type process which develops gradually over many years.

Harif Mottay: (Shareholder) I remember now he had vascular dementia.

Craig Ritchie: Yes, so that's - and I think one of the dilemmas I guess we face is that we know within our clinical practice that people exist on this very sort of wide spectrum of conditions and very different - everyone is an individual.

Harif Mottay: (Shareholder) Yes.

Craig Ritchie: So when one does a trial we have to somehow try and lump people together under a single sort of diagnostic concept and that's why we use criteria for Alzheimer's dementia and people have to satisfy those criteria. But we certainly had quite a long discussion at our Advisory Board when we met in Nice a few weeks back about whether or not Xanamem would actually be a very specific anti-Alzheimer's drug or whether or not given its profile and given the many different pathways and different disease processes that elevation and cortisol affect, including the heart, including blood flow to the brain, as to whether or not we needed to be quite so specific.

There are many other drugs in development which are highly specific to very critical parts for instance the creation of amyloid which is this protein one sees in Alzheimer's disease. Xanamem isn't that specific. It's very specific in terms of the enzyme it affects in terms of cortisol metabolism but cortisol itself has many deleterious effects when it's elevated. We talked about type 2 diabetes, we've talked about the Alzheimer's disease process and also and coming back to your father's case it may also improve blood flow to the brain which would reduce the risk of subsequent small strokes and therefore the progression. But in the trial itself we've had to specify a particular sub type and that's where we're at at the moment.

Harif Mottay: (Shareholder) Okay, thank you very much.

Operator: Thank you, there are no further questions in the queue at this stage so may I now hand back over to Dr Ketelbey for any closing remarks, thanks.

Bill Ketelbey: Well thanks very much and thanks to everybody who called in and listened in to the call and certainly to the callers who put questions to the Advisory Board. As I said in the beginning a particular word of thanks to Craig for being up beyond midnight, very much appreciated and to Jeff who may not still be online, he had to go early. But to Jeff thank you very much again for calling in from the US early in the evening.

I think just hearing the questions, sharing the answers and sharing the scope and spectrum of the questions I think it's clear the interest in the area. Equally clear the breadth of knowledge and experience that resides within the Advisory Board and for us at Actinogen this is the particular attraction and why we're particularly pleased to have these three gentlemen on our Advisory Board to help us in designing our Phase II trial for Xanamem in Alzheimer's disease. It is a complex area.

We all recognise how difficult it's been to develop drugs in this area over the years. 15 years ago or more I was involved in developing Aricept which was one of the first drugs to come to the market and still remains as market leader. It hasn't been superseded, not that it's a particularly effective drug, it's just the best there is and what it speaks to is a market that is desperately in need of more medications or more approaches to treating Alzheimer's disease. For the continuing efforts of biotechnology companies and importantly their investors in targeting this disease that is just growing inexorably year on year and within the next generation will become the biggest medical problem that all countries and societies face.

So it's particularly pleasing for us to be in this exciting new area and dealing with this compelling new opportunity as a potential treatment for Alzheimer's disease. So I thank the Advisory Board, I thank them for

joining the Board, for the work they've done at the first meeting that we had and since then in developing the protocol and for the further development that I know they will be involved in in refining this protocol in the lead up to starting the work early next year. So thanks again to everybody for calling in and thanks again to the Advisory Board.

Operator: Thank you very much. That does conclude today's conference call, you may now disconnect your lines. Thank you for attending.

End of Transcript