

## Alzheimer's Talks Transcript

### How close are we to an approved treatment for Alzheimer's? with Bernard Munos

Monday, March 31, 2014

**George Vradenburg:** Welcome to Alzheimer's Talks. Thank you all for joining us today. My name is George Vradenburg. I'm the Chairman and Co-Founder of [USAgainstAlzheimer's](#) and the convener of the [Global CEO Initiative on Alzheimer's](#). And like many of you, I've been personally touched by this damn Alzheimer's disease with the loss of my mother-in-law, a very powerful political and civic figure in New Jersey 20 years ago, who became a shell of her former self and lost control of, in the end, all of her bodily functions. It's a terrible disease. We're going to stop it.

We've got 112 people today registered from 29 states and the District of Columbia on this, so thank you all for joining us as I said.

Recent reports have shown that in fact over half a million people a year are dying of causes attributable to Alzheimer's and making Alzheimer's a rival unfortunately for number two killer in the country right after cancer. It is a cancer size problem and as you all know, the investment in this disease by NIH and by others is not at cancer size levels. At the rate we're going, we're going to lose roughly 20 million baby boomers to Alzheimer's and the cost to the country will be over 1 trillion dollars annually by 2015. Yet, there are drugs now in the pipeline being tested that could be available within the next few years, if successful.

And today we have Bernard Munos, who has been looking into the pipeline for Alzheimer's drugs now in the recent past and who has, because of his service at Lilly and in a number of different roles, is an expert in this space. He is now the Founder of InnoThink, a consultancy that focuses on pharmaceutical innovation. Specifically where innovation comes from and how to get more of it. He was previously an advisor as I mentioned of corporate strategy at Eli Lilly. His research has been published in Nature and Science profiled by Forbes Magazine. A popular industry newsletter FiercePharma has named him one of the 25 most influential people in biopharma. Bernard is a Senior Fellow at FasterCures, a center of the Milken Institute, and he serves on the Advisory Council and the Cures Acceleration Network Review Board of the NIH's National Center for Advancing Translational Sciences, to its friends it's known as NCATS. He is a member of the Institute of Medicine's Forum on Drug Research and Development and Translation and advisor to the journal Science Translational Medicine. He advises companies, non-

profits, and government-funded research organizations on how to become better innovators. In addition to discussing the drug pipeline, its status and the drugs in it. Mr. Munos will also discuss with us today his recommendations for how we can organize research more effectively so that we can get to a cure faster and at lower cost and how to lower the cost of innovation and reduce the risk of failure, so that we can get to a treatment or cure much faster.

This call has made possible today by the generous support of the Zickler Family Foundation. We are grateful for their support for this call and previous calls so that we can have these important conversations.

As a reminder, if you have a question during the call please press star 3 on your phone. By pressing star 3, you'll be placed into a question queue. Please have your question ready to share briefly with a member of our staff and they will try to get you on live to talk with Mr. Munos as soon as possible when we open it up for questions.

Bernard, thank you so very much for joining us today. We truly appreciate your time and we look forward to hearing from you.

**Bernard Munos:** Thank you George and good afternoon everyone and thank you for taking time out of your busy schedule to participate in this conversation.

Alzheimer's is rapidly becoming a national emergency and the number one societal problem that threatens to crash our economies. Its annual global cost is currently at \$604 billion and quickly headed for 1 trillion. And there is no end in sight because so far there is not much of a hint of treatment yet.

Since World War II, FDA has only approved six treatments for Alzheimer's and as we all know none of them had been very good and they've all relied on the same mechanism. The last treatment was approved in 2003. And it's not that we haven't tried. I have recently completed a survey of the industry pipeline and since 2000 more than 350 therapies have been investigated in a clinic but over 200 of them were discontinued before being even submitted for approval. Of those remaining, none so far has brought spectacular or even appreciable relief. It doesn't mean that they are not effective, it just means that we need to wait until the conclusion of the trial to get a better read. Sometimes we're lucky, you see that in fields such as cancer where you start a trial and something works so well that patients know they are getting the right drug but we haven't seen that yet in Alzheimer's. And it's not that we've lacked imagination either, over the same period of time since 2000, over 150 therapeutic strategies have been attempted involving small molecules, vaccines, antibodies, peptides, natural products, stem cells and even gene therapy. But unfortunately, we don't have much to show for these efforts yet. Most other diseases, perhaps with the exception of tuberculosis, would have been vanquished or at least partially vanquished by such assault but Alzheimer's keeps defying us. Drug R&D spending has soared as well reaching conservatively over \$25 Billion since 2000. But frustratingly all that money has produced few actionable insights so far about the etiology of the disease. Is it caused by amyloid plaque, by tau tangles, by genetic mutations, by prions, by oxidative stress perhaps compounded by inflammation, mitochondrial malfunction or metabolic syndrome, no one really knows? And yet, if we knew we could probably produce a disease modifying treatment within a few months or years at most. Our tools and

our scientists are up to the challenge, as they have demonstrated with cancer and HIV. But fewer researchers are now trying as many pharmaceutical companies are stepping away from a challenge that the fear is too daunting. The problems are many-fold: we don't know what causes the disease, disease progression is very slow, and we don't have a good biomarker to track it. The result is that the odds of success are very small, much smaller than 1% for every drug candidate that enters the clinic. How much more is impossible to say because we haven't really had any success.

So what do we do? I think it's easy to get depressed, but we should not. There are a number of things that we can do to speed the innovation and to speed the discovery of new treatment. The first one is avoid duplicating our mistakes. If you look at the trials that have been conducted in the last 15 years, many trials have involved similar therapeutic targets. And it's not uncommon to find a situation where a company has abandoned the target after spending hundreds of millions, if not billions of dollars on it. But another company is still pursuing it because they haven't seen the data of that other company and they will basically rediscover or reduplicate the mistake that was done by the first company. So I think the first thing we can do is share our experiences, our data to a far greater extent that has been done so far. So that whatever money we spend on researching treatments we maximize its utility.

We also should perhaps open our minds to novel pathways of drug discovery. One for which the industry has shown little interest so far but which keeps surprising lots of people is this idea that often times existing drugs can be used well beyond their approved claims. In fact it's been documented that for some hard to treat diseases over half of the drugs prescribed are prescribed off-label. So this off-label prescribing or drug repurposing, as it is called in industry jargon, is a way to get cut-rate innovation to market relatively quickly, within five years. And I don't think that particular pathway has been well leveraged in the quest for Alzheimer's treatment. And yet the data already exists, any large insurance company has tens of millions of patients taking just about every drug that has been approved. And by mining the data it's should be possible to identify a cohort of patient taking a particular drug and a matched cohort that doesn't take the drug or doesn't take anything for that matter. And look at the incidence of Alzheimer's in those cohorts. And the idea there is basically to get a signal. So that a signal that someone or something might be able to produce you know the desired effect so that scientists can start formulating novel hypotheses about what causes the disease and making progress faster than we've seen so far. So this sort of epidemiological study I think should be done. We have the data. It shouldn't be too expensive to do this, statisticians can filter through the noise and see if we've got a signal out there.

I think we also need to bring more brains to the disease, I mean we've had lots of smart people including some of this smartest people in the planet working on the problem. But that has not been enough. There have been other pathways that have emerged recently. One of which is crowdsourcing, which basically means tapping the global brain. And if you go around and talk to scientists around world, you have biomedical scientists that have interesting ideas about Alzheimer's, but currently they do not participate in the current discussion because their ideas are not main-stream. I think we need to bring them into the discussion. And I think we also need to invite into the discussion, people who perhaps have no knowledge of biomedical drug discovery but are knowledgeable about data analysis, about modeling, and can bring tools that we have not used in drug R&D. And perhaps help us make sense out

of the enormous amount of data that we've already gathered, that have been well under exploited. Crowdsourcing works. There are countless examples in countless different fields that suggest that it is a very powerful and economical way to crack very tough problems. We need to use it to a greater extent than we've done so far. And an ideation challenge as they call it, which means you go to the crowd and basically ask them - What's a different way? What's a better way to tackle Alzheimer's? And I think if we try that we will be surprised by the richness of the feedback that we're getting.

Another challenge in tackling Alzheimer's is that we haven't been able to reverse let alone cure to disease. And there's indication that when the disease manifests itself, it has actually been brewing for sometimes decades. So increasingly scientists believe that in order to tackle the disease we have to start way before the disease manifests itself, in a preventive way, if you will. Now that itself adds additional challenges because how to prove that a non-symptomatic patient receiving the treatment who does not develop the disease would have eventually developed the disease if they hadn't received the treatment and for regulators that's an even bigger challenge. So in order to make progress, we're going to have to harness and enroll large cohorts of patients. Basically pre-enroll them in clinical trials and use emerging technologies such as biosensors to gather thousands of physiological data points, a hundred times per day, over many years and wait until some of those people develop the disease so that we can go back to the data play it in reverse and start understanding where things got off-track. Data, I believe, can and in my view probably will help resolve the Alzheimer's challenge. This is a new field we haven't had that before I mean a whole area of biosensors and what they can do is something that is growing very fast but just about a year ago, a year and a half ago it sounded like science fiction. Regulators are working very hard in order to provide guidance on how to use all that data and a lot of people involved in biomedical research are racing against the clock to make the best use of this new field of digital health. Digital health can be a major contributor to Alzheimer's but we're going to have to all contribute our own lives and that of the people we know. We will have to volunteer to participate in that giant data collection exercise because without data we just won't be able to find out what happens during that pre-symptomatic period. We won't have the natural history of the disease when we can really make a difference.

So we're not powerless. We're not lacking of ideas but we have to do things a little differently. At the recent meeting at the New York Academy of Sciences last November there was a lot of pushback from many participants that perhaps drug R&D had been focusing on too much of the same thing. Looking into the lamp-post so to speak and there probably is some truth to that. But there are plenty of other things that we can try, that we have tried, so far we haven't really been successful. But we've got plenty more to try.

So I'd like to leave it there and maybe turn it over to you for questions. I hope that these few words have given you a balanced perspective on what has been and what it could be. I think there's reason to be cautiously hopeful that things are going to get better but we are going to have to continue working very, very hard together. Thank you.

**George Vradenburg:** Bernard, thank you so very much for those comments.

Just a reminder for everyone - if you have a question, press star 3 and by pressing star 3 you'll be placed into a question queue and talk to a member of our staff and we'll get you on the air so to speak with Doctor Munos.

I'd like to start with one that comes from some questions we received before the call, Bernard. Are there any drugs currently in the late stage trials regarding tau? That's one question and the other sort of related question is, why is that there are numbers of people with very heavy loads of beta amyloid and tau in their brain but never get Alzheimer's?

**Bernard Munos:** Yes, there are a number of treatments that target tau in the clinical pipeline no question about it. As I said, no one so far has produced spectacular results whereby IRB's basically intervene and say we've got to stop this trial immediately and make that drug available to all patients because it looks so good. We haven't seen that yet we may see it and I hope we do but at the moment we have not. It doesn't mean that those treatments are ineffective, it just means that we have to wait until the conclusion of the trial to get a clear read. The other question, I'm sorry, second part of the question was?

**George Vradenburg:** Why some people pass away with tau tangles and plaques in their brain but don't show any signs of Alzheimer's?

**Bernard Munos:** Yes and that's because there is a clear association between plaques and Alzheimer's. In other words if you have Alzheimer's you are going to get plaque. But the fact that you get plaque doesn't necessarily mean that you have Alzheimer's. Plaque is a necessary but not a sufficient condition for Alzheimer's. So we don't know in effect whether it is causative or whether it is an outcome, it is correlative. And in spite of all the money that we've spent and all the trials that we've done we still do not know that. Some companies Merck in particular, have started recently some trials that they hope will bring the final answers to that question. But at the moment we don't know and therefore we may well have pursued the wrong targets. I mean it sounded like the right thing to do at that time but since we do not know the etiology of the disease treating the consequence instead of the cause may be the reason why those treatments haven't worked.

**George Vradenburg:** Thanks, we have a question here from Carla Danesi. Carla, would you ask your question please?

**Question:** Hi yes, George hello and I love you and everyone there. I believe you know who I am and you know my mom's story and you know that I've been hot on the tail for a new medicine for my mom for practically 15 to 20 years. And just in my own personal research I just want to bring to everyone's attention J147. J147 has been very much the underdog in all of this and I don't know why. I've been following it very, very closely, Doctor Schubert is working on it out of the Salk Institute and he's currently in IND. He showed great promise in all of his preliminary tests including toxicology and now he's going into histology. And I started the dialogue with him several years ago in fact just to keep up on how he's doing and he is currently trying to go into phase one. Like everyone else he's having some problems securing funding. However, his compound is increasingly promising and I just want to bring it to everyone's attention because I really think it needs more focus. It is something that I am very very

securely wanting for my mom and I would give it to her tomorrow. In my own quest as a layman I've always looked for anything that would not make her brains swell, make her turn yellow or make her vomit and anything that I felt that would actually help the disease without harsh type effects. So I think that this is something that we really need to focus in on that and also the Insulin nasal spray, which I know we have talked about in the past. So I just wanted to bring that to your attention and just get some input on that and some feedback and see everyone has to say. Thank you George.

**George Vradenburg:** I'd be curious, Bernard, you are certainly aware of the SNIFF trial but J147, I'm just curious as to your assessment of those therapeutic products.

**Bernard Munos:** Well several comments. The first one is that we're dealing with something that is pre-clinical and at that pre-clinical stage, over 90% of the molecules die at that stage so the failure rate is quite high. Now that doesn't mean that this particular treatment will not make it and I hope it does and I'm encouraged by your enthusiasm. I think we're going to have to see in order to get a clear read since animal models have been rather unpredictable in the past, I wish you're right. I've talked to other scientists that feel the same level of passion regarding other treatments. Recently I had a very intense conversation with someone who was convinced that mitochondrial dysfunction was the culprit in Alzheimer's and had all kinds of evidence to quote and I hope he's right too. We're not even sure whether Alzheimer's is one disease or one phenotype that is the end result of multiple methodological processes in which case having you know various treatments targeting various pathways might be appropriate. So I'm excited to hear what you have to report and I'll keep an eye on it but we'll have to see until some patients gets treated in order to confirm that we're really on to something that can deliver.

**Question:** Thank you.

**George Vradenburg:** I just wanted to thank Carla. Carla has been a very, very active, raising her voice and telling her story and just wanted to thank her for speaking out. Not everyone is as energetic and as passionate as you Carla, at least not able to express themselves so well. Thank you for what you do.

**Question:** Thank you.

**George Vradenburg:** We got a question here from Cassandra Brenton. Cassandra, would you please ask your question. Cassandra? All right let's move on to Marilyn Flint. Marilyn, would you please ask your question.

**Question:** ..From Alzheimer's lead me to discover some natural remedies as well as pharmaceuticals. Gary Wenk, a professor of Neuroscience Immunology and Medical Genetics at Ohio State has studied how to combat brain inflammation for over 25 years. And he has found that cannabinoids in the cannabis plants are the only thing that he has found to work in reducing this brain inflammation. You probably know that with the hemp oil there's no THC to make you high as there is in marijuana oil and they're finding that is helping in ALS, Parkinson's disease, AIDS, dementia and Multiple Sclerosis, Autism and Schizophrenia. A National Institute of Health Study acknowledges that these cannabinoids provide an unrecognized molecular mechanism through which these debilitating diseases can be affected. I'd like

you to comment on, how you're commenting on the drugs that are being tried, but what about these natural remedies that many studies, there are nearly 2 million sites about that on the internet are finding that these natural remedies are very effective.

**Bernard Munos:** There are quite a few natural products that have been tried and were included in these 350 therapies that I mentioned in my introduction. Natural compounds have historically been a very rich source of effective treatments for all kinds of diseases. So trying them out for Alzheimer's is certainly the right thing to do whether they can bring something will have to see. So far there has not been anything spectacular that has been reported involving natural remedies. It doesn't mean that they are ineffective it just means that we need more data in order to better understand whether we do have a therapeutic effect or not.

Now I'd like to add that when you looking at the problems of Alzheimer's there's various aspects to it. Alzheimer's when it is in its clinical form basically results from degeneration of the brain. You have loss of brain mass and therefore the delicately organized network of neurons that is the hallmark of the normal brain has been degraded to a point through the demise of neurons has been degraded to a point where the brain is no longer effective. And regenerating the brain mass or somehow stimulating neuron growth to the point where that the network of neurons can regain something that approaches its original structures is quite a challenge. I mean that's where a cure would come from. Now you'll also have treatments that considerably could alleviate the symptoms of Alzheimer's and not bring a cure but perhaps bring the deterioration to a stop and alleviate the symptoms and natural products may potentially do that. I'm not aware of any that do although there's many claims out there but unfortunately I would be little careful about those claims because Alzheimer's is such a huge problem for patients as well as for governments the world over that if something works as well as sometimes represented there's no question that the particular treatment would be embraced immediately by millions of patients and it would be all over the news reports. The fact that the many of those things tend to be you know, confidential, word of mouth and website and so forth suggested perhaps and unfortunately it is not quite as spectacular as we would like to them to be.

**George Vradenburg:** Thank you. Next question from Michele DeSocio, I hope that's the way you pronounce it. Michele, would you ask your question please.

**Question:** Hi. Quick background, my mother is now 73. At age 58 she was misdiagnosed with bipolar disorder lived with me for many years. After five years of medications she was diagnosed with either Pick's, Frontotemporal lobe or Alzheimer's they don't know she is currently in the late stage. My question is - many people are treated with anti-anxiety medications or depression medications before diagnosis. Even caregivers for stress are also treated with medications and they are also subject to possibly getting the disease with the family history of early onset. How will these medications affect the trials?

**Bernard Munos:** Let me make sure that I understand the question. How medications that are targeted at other neurological diseases such as depression or schizophrenia may impact an Alzheimer's trial?

**Question:** Yes.

**Bernard Munos:** Okay. I certainly don't have the answer to that question and I don't if anyone does. The mental illnesses are still poorly understood and poorly treated and the interaction between mental illnesses is something that is equally poorly understood. I wish I could provide some insights but unfortunately...

**Question:** Will they be disqualified from the trials while being on medications?

**Bernard Munos:** Well clinical trials usually have very strict exclusion criteria and typically being on other medication is often an exclusion criteria. Now each trial has their own criteria and it would depend upon the trial design, the treatment under consideration and all kinds of other factors. So I don't think the general rule would apply. It would have to be looked at on a case by case basis. But to untangle the interaction between mental illnesses and potential treatments is something that is very, very difficult and I don't know whether anyone would have or would claim to have a satisfactory answer to that question. I wish I could be more helpful but this is you know, part of the huge grey area that we have not yet been able to penetrate very effectively.

**Question:** Yes, unfortunately many people take 5 to 10 years before they're diagnosed and they are seeking treatment and they're getting mistreated because of their age and Alzheimer's or dementia is not the first thing that comes to mind because of age and they're treated with these drugs you know, wrongly.

**Bernard Munos:** You're absolutely right and unfortunately they couldn't be treated with Alzheimer's because apart from the six treatments that I mentioned earlier which brought very temporary relief there is at the time today we haven't found something that is effective enough for FDA to approve. So what I think happens when people are giving those other treatments is an attempt to treat the symptoms because anxiety is often times accompanied or accompanies the pathology of Alzheimer's. So you have such attempts but it does not modify the disease unfortunately.

**George Vradenburg:** I think that's a good question. It actually raises an interesting alternative question and that is if I was a person with MCI, mild cognitive impairment or very mild Alzheimer's, do I care whether a potential treatment is disease modifying or whether it simply suppresses the symptoms of cognitive or functional loss? In a sense there are other conditions that we accept be anything as trivial as a cold or cancer that is in remission but is not cured. And so if I know that some of the symptom treating products on the market are limited in the dosages that you can take because of the side effects, but if one could suppress the side effects and up the dosage, might one find a treatment that would have a dampening effect on symptoms for a much longer period of time. That is to say from a patient's point of view, do I care whether a treatment is disease modifying or whether it is symptom suppressing?

**Bernard Munos:** I think you should care whether it is disease modifying because the reality behind Alzheimer's is that you have gradual loss of brain mass which affects the structure of the network that connects all those neurons which causes Alzheimer's and all its manifestations. So this is the process that needs to be stopped if we are to stabilize a patient and produce long-term alleviation of symptoms. So this is why it is important to have a disease modifying treatment so that this brain loss is stopped and ideally reversed, although that's an even taller challenge. Now, if we cannot do that we can probably

find something that will make the disease more bearable but I think it will provide only temporary relief because at the end, we'll have to reckon with the fact that the brain is wasting and as neurons get lost the patient's condition will only get worsen.

**George Vradenburg:** Okay, thank you. Just as a reminder if you have a question, please press star 3 on your phone and by pressing star 3 you'll be put into a question queue and will after some conversations with our staff about your question get put on the air with Doctor Munos. Cassandra, I think I've called you out before. We've lost you, are you on the line now and do you have a question? Cassandra? We are having trouble with Cassandra. She's been on twice to ask a question, twice.

I'm going to ask a couple of questions that have come in before this call. Why is Alzheimer's in your view at the bottom of the list for funding for research - I'd be curious as to your view on that subject.

**Bernard Munos:** Yes, you know I think traditionally there have been two different pathways to discover new treatments for diseases. In the first one, we just throw molecules at the disease hoping that we are going to get lucky and something is going to work. And it sounds maybe a little crude but that historically has worked reasonably well and has been the source of many effective treatments for diseases. So that's one way to go about it and pharmaceutical companies have libraries of molecules that reach well into the millions together so is quite a formidable force and that has been used and fortunately not successfully. Now some people now saying well which we really did it late, we should have done it earlier and so forth but it remains that process has not worked. We have not been lucky. We have not seen really meaningful improvements.

The other pathway is try to understand the etiology of the disease that we're dealing with so that we can act intelligently so to speak upon that etiology in order to stop the disease process. And that has been tried but so far we have not really been able to unravel the etiology of Alzheimer's. As I mentioned earlier, we don't really know whether it is due to amyloid, to tau, to prions, to inflammation, to mitochondrial dysfunction and depending upon which of those hypotheses are correct you could have one or the other treatment. So what we've seen recently is that some companies after banking large amounts of money onto hypotheses that did not produce successful clinical trials have basically backed off and said, we really need to understand what we're doing here before we continue to throw money at this disease. And you cannot really blame them for taking that stand. Throwing money is not necessarily going to lead to a solution. We need to understand what we're doing. So some companies have kind of retrenched to some extent from Alzheimer's are still interested in it but their efforts at the moment are more towards understanding the disease process so that they can identify ways in which pharmacologically we can interfere with the disease process and come up with something that would modify it.

So I think from what I've gathered there's no lack of interest in industry or at NIH for that matter. It still remains a priority but I think they're taking maybe a smarter approach which is no longer brute force which is more let's try to understand what we are dealing with and I think as we're making progress in deciphering the pathology of Alzheimer's I think we will see the reinvestments from pharmaceutical companies in this disease.

Now I mentioned earlier this idea of ideation challenge on a platform such as Innocentive, and the evidence suggests that such a challenge would probably produce a profusion of ideas that have never been considered so far that could potentially bring a solution to Alzheimer's. This is the hallmark of crowdsourcing, it brings into the fray so many minds that are wired so differently that are taking different approaches to solving problems that each yields insights that have not been considered so far. So if we were to run such a challenge, I'm sure we would find a lot of novel ideas and novel pathways that could be tried, which might bring back a renewal of investment into Alzheimer's - and some of those frankly could be based upon this drug repurposing pathway that I mentioned earlier, this idea of using drugs that have been approved for other diseases. It could be inflammation drugs, could be all kinds of stuff. Sometimes it is completely unrelated and using them in order to test some novel hypotheses and hopefully finding something useful in the lab. It would not be the first time. So I'm optimistic about this.

**George Vradenburg:** So Bernard I am going to take that idea up with you offline after this call because I am intrigued by it and seeing whether or not we should follow up on it.

**Bernard Munos:** Okay.

**George Vradenburg:** Okay Cassandra - this is your third and last try. She apparently had her line on mute and she was yelling at us. You have your question.

**Question:** Yes sir, I am sorry. I have been a caregiver for my father and mother ... my mother had the dementia because of Parkinson's and my father had Alzheimer's. What I'm wanting to know is what are we doing to diagnose non-symptomatic patients and how reliable is genetics in possibly enabling us to do this?

**Bernard Munos:** This is a very good question. I don't think we are, to my knowledge I don't think we're doing much to diagnose asymptomatic patients. We certainly don't have a natural history of Alzheimer's in pre-symptomatic patients and we need it badly. Until we get it I think it's going to be very difficult to understand the disease process, to understand where we might be able to interact in order to modify it. Medicine today starts when people get sick and for some diseases unfortunately when people get sick, it's too late and Alzheimer's has been one of those. So in order to solve it we're going to have to look at people who aren't sick and you know this is difficult to do and this is where all of us who are concerned about Alzheimer's can perhaps make a difference by encouraging the people who are close to us to enroll in Alzheimer's monitoring trials. Not only aging people, but teenagers, adolescents, young people, young adults. So that we can collect data over a number of years and start seeing signals that might help us to understand what's going on there. So until very recently frankly we didn't have the technology to do this. But the technology is getting better at a very fast rate. I mentioned that in my introductory comments, if you follow that field of biosensors, wearables, plug-in devices, and so forth. You know there are breakthroughs, announcements, literally every other week. Centers have been created at major universities, companies such as Samsung and Apple are getting into the field and that's very good because for the data to be successfully collected it needs to be collected effortlessly and at no cost and basically those biosensors allow us to do that. So I expect some major progress to arise from that

technology the fact that we can have thousands of data points collected about each one of us every day at no cost will help clinical research in general for all diseases. So I think it will be a major development and we're almost there certainly in the next year or two I think we'll be there. So that's one opportunity that we haven't had yet, that's now opening to us and we should seize it.

**George Vradenburg:** Next question from Mary Norman in Mocksville, North Carolina. Mary?

**Question:** Yes, I wanted to know if you have any information on the SNIFF study, the Insulin study. My sister and I are doing that right now. My mother and older sister had passed away with Alzheimer's and I have another sister that's in a nursing home with Alzheimer's and we certainly are getting at the age that they were when they got it and we're very concerned and are taking part on that study. Do you have any information on that study?

**Bernard Munos:** I do not. I mean I'm aware that those treatments exist that they are in a clinic. As I said, no one has emerged as being you know cured or significantly improved as the result of those treatments so we haven't had the situation yet, it does not mean that treatment is ineffective. It just means that we have to wait until the conclusion of the trial in order to get an accurate read. It's based on a valid hypothesis, a lot of intelligent people are behind those hypotheses so we cannot dismiss them and we can only hope that something will come out of it. But at the moment it's too early to tell.

**Question:** Okay, thank you.

**George Vradenburg:** Next question actually is from Peggy Brick in Kennett Square, Pennsylvania. Peggy?

**Question:** Yes, I'm curious as to your response to Peter Whitehouse's rather incendiary book called The Myth of Alzheimer's in which he who was a major researcher, is very sad and upset about the growing of what he calls an Alzheimer's empire what he calls an Alzheimer's industrial complex of the marketing of all kinds of things that he thinks are not useful and in fact as I'm hearing you are not... do you know of Peter Whitehouse?

**Bernard Munos:** I don't know him but clearly there are a lot of people who speak about Alzheimer's and want to be active in it. There's critics and there's people I mean you know, it's a complex ecology, I would say that. I don't think there's any conspiracy to refrain...

**Question:** Not a conspiracy but rather an inappropriate marketing of people who are really trying to get into this not in a helpful way necessarily but simply in a financial way.

**George Vradenburg:** I think Peter Whitehouse's theory, Bernard, is that there is no such thing as Alzheimer's it is simply natural aging and an effort to try a label it a disease in order to permit the marketing of drugs aimed at natural aging is simply an effort to make money out of a mythology that there is something called the disease called Alzheimer's rather than normal aging.

**Bernard Munos:** Yeah. Well you know I don't think there's any shortage of people trying to make money out of Alzheimer's in various ways. But in this particular case, I think science has debunked that proposition. I think it clearly shows that you look at under the microscope at the brain of an Alzheimer's

patient versus a brain of someone of equal age that doesn't have Alzheimer's and the difference is striking and you can find them all over the place on the internet. So there is solid evidence that we're dealing here with a geriatric disease that is a real bonafide disease. The fact that people want to make money, it's not surprising, it is a national emergency, it is a global crisis and every time you've got those kind of priorities you're going to find all kind of shady characters trying to take advantage of it. As well as you know honorable people trying to do some good as well. I think it's up to us to criticize our judgments and make sure that we work with the right kind of characters. But to answer your question, I would disagree with that proposition Alzheimer's is all to real unfortunately and we've got to reckon with it.

**George Vradenburg:** So there's a question here that came in just before the call and the questioner asks, if we could identify, or someone could actually identify a drug that was safe and had signals of being effective, is there a way that we can get it through the FDA without going through so many multiple trials and taking so long?

**Bernard Munos:** Yes, I would be quite optimistic about this, FDA under the current leadership has become very innovation-friendly. There's no question about that, they created pathways such as breakthrough designation, a pathway that allows drugs that are targeted at diseases with high unmet needs, and Alzheimer's probably the disease with the highest unmet need to get to the market quickly and you know, on the basis of whatever evidence has been accumulated that suggests there is a positive treatment response and the rest of the research is being done you know, following the drug introduction. That pathway has been implemented in the last year or so several times, it seems to work as expected. So if we were as lucky as to find a drug that would fit that bill I've got no doubt that the FDA would be keen to bring it to the market as quickly as possible.

**George Vradenburg** We've got time for one more question, Michael Ellenbogen is one of our most articulate early-onset disease people. Michael, what's your question?

**Question:** Yeah, I have a question and I guess kind of comment. Are you familiar with a gentleman named Donald E. Moss. I came across him a while ago and I thought he had something very good yet the person has been unable to get funding for something that I kind of believe might be a possible cure its called MSF. Do you know anything about that?

**Bernard Munos:** No, I do not. But I wouldn't be surprised frankly because in science you do have, fashions and fads and we've seen one in Alzheimer's with the amyloid hypothesis for example and those fashions and fads unfortunately drives much of the funding and if you sometimes want to challenge the accepted wisdom, that attempt to follow those fads it becomes very difficult to get grants, to get money. So you know you would think science would be very objective and unfortunately that's not the case and there is perfectly valid hypotheses out there that deserve to be investigated that might even do some good and possibly a lot of good that aren't supported because there's a tendency in drug R&D to fund safe research as opposed to breakthrough research and this is one thing where all of us you know, the patient community and the patient advocates can help make a difference by rattling Congress because ultimately that's where it comes from, rattling Congress and imposing upon our representative that we

need to be bolder in what we fund, we need to move away from our comfort zone, fund breakthroughs from science and not so much safe science. The hallmark of science, the point of it is really to explore it's not to validate whatever ideas we've already researched. So you may be onto something, that particular person may be onto something. It certainly wouldn't be the first time it happens in science a lot of the major breakthroughs were first derided as funky ideas I think we need to seriously consider all the funky ideas that we can find about Alzheimer's because one of them may hold the answer to this challenge.

**Question:** Thank you very much Dr. Munos. We really appreciate you sharing your views with us today. He and I did not rehearse this but you all will be receiving an e-mail from me tomorrow because the Senate co-chairs of the Alzheimer's Task Force, Senators Collins of Maine, Warner of Virginia and Markey of Massachusetts are sending a letter to the appropriators urging them to provide another incremental year over year increase in Alzheimer's funding at NIH and we need to have all of you talk to your senators in your states to sign on to this letter to provide the kind of momentum for that additional funding that Bernard has mentioned because with that additional funding we can pursue not just the mainstream ideas but novel ideas. But if we have limited funding, the limited funding will tend to go to the tried-and-the-true but with additional funding we can try the greater number of wild duck theories. So you will all be getting an e-mail from me tomorrow urging you to call your Senator's office.

Again, I want to express my thanks to Bernard Munos for his time today. We are grateful to the Zickler Family Foundation for sponsoring this call. Thank you all for participating in this Alzheimer's Talks. In about a week we'll have a copy of this recording and a transcript on our website for you to share with your friends or to listen offline, we find more listeners off of the website actually than on these calls and that's in large part because of people's schedules. But in fact, the website does allow you to listen to these calls sort of offline as it were.

As always, please stay on the line if you'd like to leave us a message with a question or comment please let us know what you've thought of the call and what you would like to have discussed on future calls.

So thank you again Bernard Munos for sharing your time today and your thoughts with us and thank you to all the participants on the call. Have a good day. Bye-bye.

**Bernard Munos:** Thank you.