UsAgainstAlzheimer's

Alzheimer's Talks
with Dr. Scott Turner
January 25, 2017

Note: Transcripts are edited for content and clarity.

George Vradenburg: Welcome to Alzheimer's Talks, a free monthly teleconference presented by UsAgainstAlzheimer's, connecting you with leaders working to stop Alzheimer's. My name is George Vradenburg, Chairman and Co-founder of UsAgainstAlzheimer's. I'm here today with a member of our board, Karen Segal from Chicago.

UsAgainstAlzheimer's is a patient-powered venture philanthropy, an entrepreneurial and innovative organization which is disrupting existing practice and the way we've done traditional business in the Alzheimer's field in order to get to a cure faster.

Just a couple news pieces. For this particular audience this may be old news, but we did have a drug failure at the end of 2016. Solanezumab, what was thought to be a promising disease-modifying drug against Alzheimer's turned out not to be successful. I should say, that's not the right way to put it because it was a negative trial. In a sense, it did show success because it did show its ability to reduce through time beta amyloid, but the results of reducing it were not sufficiently strong that it was regarded as a material clinically meaningful result. It reduced the rate of decline of the disease by about 10 to 15 percent on a number of measures. We, and they, were looking for a more powerful drug.

We did learn a lot. We learned that the drug did attach to amyloid and that in fact on some measures it did reduce the rate of decline suggesting to at least Lilly and others in the field that we either should go earlier so that a modest rate of decline can have a major impact through a longer period of time or we ought to be thinking of higher doses if we can find ways to do that without adverse side effects. We learned things, that's why I hate to characterize this as unsuccessful, but on the other side it was a negative trial.

We do have a change in administration in Washington D.C. as probably everybody knows. We are one week into, or a little less than one week into, the Trump administration which means that everybody in this town changes their chairs. The Democrats are selling their homes and moving out, many of them, and the Republicans are buying homes and moving in. As a result, a lot of changes obviously at the top of the administration and we're getting to know the people that are coming to town and learning their preferences. Intriguingly, Tom Price, the candidate nominated to head the Health and

Human Services Department asked about his intention with respect to Alzheimer's confirmed that he would like to make it a priority as well, which continues the preferences and priorities of a Republican congress. We're hopeful that this administration will, like the last administration, continue to prioritize Alzheimer's, but given the uncertainties on the overall budget and how much will be allocated to defense and to domestic discretionary spending we do not know.

An interesting little piece of news today, David Cameron the former prime minister of England who basically launched the G8 effort against Alzheimer's, was just announced as President of the Alzheimer's Research U.K., which means that this former Prime Minister and head of state is going to continue to devote time and attention to the Alzheimer's cause. So that's a good piece of news.

Today our guest is Dr. Scott Turner. Dr. Turner is a Professor of Neurology at Georgetown University Medical Center and the medical co-director of Georgetown Translational Neurotherapeutics program and director of the Memory Disorders program. A number of positions which center him in the midst of the fight that we're all engaged in against this disease. He is one of the nation's foremost clinical researchers and he leads research in Alzheimer's disease at Georgetown.

He is going to talk today about an exciting clinical trial that he has just launched at Georgetown University utilizing and repurposing a cancer drug as a possible treatment for Alzheimer's disease. There is a parallel study repurposing the drug for Parkinson's as well which he can refer to, although, Dr. Turner is charged with the Alzheimer's trial. He's going to share information with us on this clinical trial, why he thinks this particular anti-cancer drug that's already on the market, could be a possible treatment for Alzheimer's, and the concept of drug repurposing and the extent to which Georgetown is involved in a wide variety of trials in the Alzheimer's space.

At UsAgainstAlzheimer's we have a goal to find a treatment faster by reducing the time and cost of clinical trials so on these Alzheimer's Talks calls, we've featured many clinical trials that are recruiting participants to not only share with you the most up to date information on the science from leading Alzheimer's researchers - as we are today with Dr. Turner - but also in the hope that some of you will be interested in participating, something that we can all do to help find a cure.

I would note that today we have close to 1,000 people who have registered for this call or the recap, and we have representatives from 33 states and the District of Columbia.

Philanthropy is very important to all this work. The study Dr. Turner will describe is supported by private philanthropists, one of whom I know personally and who is on the phone, whose name is anonymous, in addition to a large grant from the Alzheimer's Drug Discovery Foundation - this is Len Lauder's organization that invests in promising early-stage clinical trials of new and novel ideas. Congrats to the ADDF and to the private philanthropists who are investing in this novel trial.

As a reminder about questions, if you have a question during the call please press *3 on your phone. By pressing *3, you'll be placed into the question queue. Please have your question ready to share briefly with a member of our staff or if you're listening to us online you can type your question in the box. We'll get to as many questions as possible after the opening presentation from Dr. Turner. Please note that Dr. Turner, like all of our guests, is not able to answer personal medical questions.

Scott Turner, thank you so much for joining us today. Thank you for the work you're doing generally, and thank you for this intriguing new innovative trial on this repurposed cancer drug.

Dr. Scott Turner: Thank you for the opportunity to talk today about these trials. We're very excited and this is also very timely because we just started recruitment last week for the Alzheimer's trial and the Parkinson's trial. Before I get to that, I just want everyone to know that we provide clinical care at Georgetown for older individuals with memory problems and dementia so the first step, of course, to getting into research is to get an accurate diagnosis. Then we prescribe approved medications, and then if someone is eligible and interested we start talking about our research opportunities. Of course there are a lot of barriers to getting to research that we try to minimize as much as we can because we also have a challenge in recruitment for these clinical trials.

We did have a big failure last year in the Solanezumab trial. We were very disappointed in the results and as a result of that failure, the drug is really no longer being investigated in Alzheimer's disease, but it is still being investigated as a prevention for older individuals who have a positive amyloid PET scan and this is called the A4 trial. You'll probably mention later on that there's a television program at ten o'clock tonight on PBS called Every Minute Counts and this gives you a lot more detail about this prevention trial of this anti-amyloid antibody.

We have many opportunities for research. We have opportunities for normal older people who are 55 or older or 65 or older, who are completely healthy to perhaps participate in a prevention study, and of course if someone has memory problems such as mild cognitive impairment or early Alzheimer's disease we have several research opportunities. Most of these studies are focused on anti-amyloid approaches, or anti-amyloid antibodies, or drugs to block amyloid production. Even though we've had lots of failures I think we're excited in the field that we think we've never been closer to actually finding a treatment so I still remain optimistic.

Some of these trials will finish this year and we will have a readout, for example, from a large study this summer. There could be perhaps some good news this summer. In addition to drug treatment trials we have observational studies. We're looking for new biomarkers for Alzheimer's disease and memory decline with aging. There's no experimental drug involved, it's just things like MRI scans and PET scans of the brain, spinal fluid collection, blood tests, other methods to try to help us figure out the disease process better. I think probably the biggest breakthrough we've had in the last ten years has been amyloid PET scan and tau PET scan.

Before the discovery of these PET ligands so that we can actually see the pathology in a living person, we had to wait until someone died and look at their brain at autopsy to look at the plaques and tangles. Now within the past ten years, and even newer for the tau PET scans, we can actually see the pathology while someone is still alive. I think this is getting us closer and closer to actual effective treatments and prevention strategies.

Let me talk about one trial that we have going on at Georgetown, and this is a cancer drug that's been repurposed for Alzheimer's disease and Parkinson's disease. The reasoning behind this was that this drug that we're trying in a clinical trial is called nilotinib, it's also called Tasigna, and it's been on the market already for chronic myeloid leukemia for the last eight years. This class of drug has really been a breakthrough in treatment of leukemia. They're very effective in maintaining someone in a cancer-free state for many years. We don't really know the long-term effects because they haven't been around for that long, but they certainly were a breakthrough.

The mechanism of action is that they promote something called autophagy. Autophagy means that the cell is basically eating itself. All the cells in our body turn over the proteins that are a part of the cell and this is just a normal process of events. You have to continually make new proteins in the cells and you have to get rid of proteins, and so this normally occurs and no disease happens. In cancer, however, if you can promote this autophagy you can convince the cell to digest itself and basically kill itself. This is the mechanism of action of how these drugs work for cancer. Now if we give much lower doses, we can convince cells that have protein aggregates that are abnormal and cause neurodegenerative diseases to promote this self-digestion of these protein aggregates.

For example in Alzheimer's disease, the amyloid builds up in the cells and in the brain and tau protein builds up as tangles. If we give lower doses of these drugs such as nilotinib, we can convince the cells to basically self-digest these protein aggregates that are toxic. This has been shown with experimental animal models by Dr. Moussa, here at Georgetown University. He's used different animal models of Alzheimer's disease and Parkinson's disease and other animal models and shown the very striking effects in treatment and prevention of neurodegenerative diseases in mice.

Since this drug is on the market we know a lot about the safety. If you can repurpose an existing drug, it will greatly accelerate its track to another purpose, for example Alzheimer's or Parkinson's disease, because so much is known about the safety and toxicity and tolerability of these drugs. Whereas if you started out with a new drug you would have a ten-year track of discovering what sort of toxic side effects the drug may have. If we can repurpose an existing drug on the market then we think this will greatly accelerate its pathway to approval for neurodegenerative diseases.

Based on the promising preclinical results with the Alzheimer's mice and the Parkinson's mice, Dr. Moussa and Dr. Pagan at Georgetown did a pilot study of patients with Parkinson's disease, Parkinson's disease with dementia, or Lewy body dementia. They were all examined in this small pilot. It was only 11 patients and there was no placebo group, there was no group that got a placebo

pill. It was all what we call open label, so everyone knew that they were getting the experimental medication. There was no double-blinding so nothing was blind, everyone knew, but this is just a phase one pilot study just to prove that it's safe and may have some indication of efficacy. This study was published last summer from the pilot and it looked very promising. It was certainly very safe in the Parkinson's disease patients.

The major side effect of the nilotinib is potential EKG abnormalities and heart rhythm abnormalities and this was not found with the Parkinson's trial. There was some evidence that it looked like it may be having a benefit for the patients, even this small group of 11 individuals. People were critical and said that this certainly could be a placebo effect, and they're absolutely right it could be a placebo effect, which is why we need to do the next trial which is the double-blind placebo control trial. That's the one that just started last week, so with the Alzheimer's trial and the Parkinson's trial we will enroll individuals and half of them will get placebo and half of them will get drug.

The treatment duration is 12 months. There are approximately 15 visits during the 12 month period. A lot of these are just to make sure that the drug is safe and so we're doing a lot of EKGs to make sure that there are no cardiac problems with the medication. Of course we're looking for not just safety and tolerability of the drug in Alzheimer's and Parkinson's patients, but to see if this does have a benefit in a placebo control double-blind study. We will look at the cognitive outcome measures, memory and thinking task, and motor outcomes measures in the Parkinson's trial, in addition to studies such as MRI scans and PET scans, spinal fluid collection, etc. to gather evidence that the drug may be effective.

Both of these are phase two trials so this is not the final large multicenter phase three, which is required for Alzheimer's and Parkinson's drugs to get towards new drug approval by the FDA. If these are successful for the Parkinson's and Alzheimer's, then we would go on to do a larger multicenter phase three trial for Alzheimer's and Parkinson's. That's sort of the strategy that we're looking at now. We have a two-year deadline for the Alzheimer’s study to get everything completed and there's one year of treatment, which mean we have to recruit our last patient to the Alzheimer's trial by November of this year. Basically looking for a volunteer to join the study every week between now and November for the Alzheimer trial, so that's going to be a challenge.

We're very excited as you can tell. This is a strategy that's brand new, that was developed at Georgetown University. It's not really being investigated in other places yet, but certainly I think other places are looking to see if this is effective and if it is then many other places will join in this as well. There are other drugs as well that are approved that work by similar mechanism. There's several of these secretase inhibitor drugs that are already approved for different cancers and so they may be investigated as well. That's the quick summary of all of our activities here. We're doing a lot of studies, investigational studies, observational studies as well as new drugs. We're doing a lot of amyloid PET scans and tau PET scans to look to see what effects these drugs may have.

Then we're doing our single site nilotinib trial to see if this is effective for Alzheimer's disease in a totally new strategy. We think it will work not just against the amyloid in the Alzheimer's brain but also against the tau and tangles, so this makes it somewhat unique because almost all of the other approaches are only anti-amyloid. The anti-tau approaches are much further back in the pipeline in the animal models and so we don't really have a good anti-tau strategy. There was a large tau trial that reported out last year that was also a failure and did not show any benefit. Last year we were all sort of depressed from this large failure of the amyloid trial as well as the tau trial, but we still have a lot of exciting things in the pipeline.

George Vradenburg: I just want to remind everyone if you've got a question please press *3 on your phone and have your question ready. A member of our staff will talk to you, we'll get you on with Dr. Turner.

Just some quick questions so I'm clear, this is a single site study so this is being conducted right now only at Georgetown. Or both of these studies actually?

Dr. Turner: That's correct, yeah.

George Vradenburg: How many participants do you need in each of those studies?

Dr. Turner: For the Alzheimer's trial we're looking for 42 volunteers to join the study. As I said, it's 15 visits within 12 months. For the Parkinson's trial it's a little bit larger, I believe it's about 68 individuals to join that study.

George Vradenburg: What stage of Alzheimer's and what stage of Parkinson's do you need to be in to qualify for your trial?

Dr. Turner: For the Alzheimer's trial it has to be definitely diagnosed with Alzheimer's disease. It's not a trial for the precursor and the mild cognitive impairment, and it's not a trial for the more advanced patients. We hope to get people just as they're diagnosed with Alzheimer's disease in their earliest stage. We think this will be when the drug will be most effective, and the same for Parkinson's disease. They have to be diagnosed with Parkinson's disease, but in the earlier, the mildest, stage of the disease.

George Vradenburg: We've got a question online about how to spell nilotinib.

Dr. Turner: How to spell nilotinib is N-I-L-O-T-I-N-I-B.

George Vradenburg: Have you nicknamed this trial?

Dr. Turner: We have not yet come up with a cutesy acronym for either one of them but if anyone has any suggestions we'd be glad to hear it.

George Vradenburg: There you have it audience, if you've got a good suggestion for Dr. Turner on what to call the Parkinson's and the Alzheimer's trials please let us know because nilotinib is not an easy roll off the tongue word.

Dr. Turner: That's correct, yeah.

George Vradenburg: This may be a very naïve question, but it strikes me that if you're introducing a drug to regulate the degree to which a cell is consuming its excess proteins, you need to be pretty careful. Careful may not be the right word, you need to be pretty accurate in the dosage because if you overdose then you're going to eat all of it. That's not good. If you underdose, you're not going to eat enough of it, that's not good. Am I right and how would you address that issue?

Dr. Turner: Yeah, you're absolutely right. We're using doses that are much lower than those used for cancer. There are two reasons for that. One is that these are the doses that were effective in the animal models, and also we don't want to get into the higher doses where there were safety concerns with the EKG and the cardiac rhythm abnormalities. We're using the smallest pill that is available and we're buying this drug off the shelf just from the pharmacy.

We're using the smallest pill that's available, that's 150 milligrams, and giving it once a day for six months, and then after six months we'll increase the dosage to 300 milligrams or two pills once a day for another six months. We'll be testing two doses, but these are two of the lowest possible doses in the range and I think this will probably be the sweet spot where we show efficacy and don't run into safety concerns.

George Vradenburg: We have a question here from Joanne online. What kind of clinical trials have to be done to satisfy the FDA in order to permit them to approve a repurposed drug?

Dr. Turner: That's a great question. To get to a new drug approval, the FDA looks for phase one, phase two, and phase three trials. Phase one and two are mostly focused on safety, and then phase two and three begin to look at effectiveness of a new medication. Once a drug is repurposed, you can skip over the phase one because that's usually done in healthy, control, normal individuals and so, of course, that was already done for nilotinib since it's already an approved medication. It allows you to fast track drug development and go straight to phase two so you have to do a phase two trial of this drug that's already available in the disease that you want to study.

The trials that we're doing are phase two trials in Alzheimer's disease and Parkinson's disease, and this is collecting information on safety and effectiveness, and somewhere between 50 to 100

individuals typically, sometimes less. Then if it's shown to be safe and looks like it will be effective, then you launch into a much larger phase three trial. For an Alzheimer's trial this typically involves more than 1,000 participants, which means that there have to be many different sites that are involved in a phase three trial. For an Alzheimer's trial also the minimum duration is about 12 months. It takes us that long to figure out if something is really affecting the disease course. That's the timeline. You have to have successful phase one, two, and three trials.

If the drug is shown to be safe and effective in the phase three trial, then you can do a new drug application to the FDA. The FDA reviews all of the data and determines whether it's approved or not. If it's approved then it would become available for prescription use. As I say, you can shave at least ten years off of the drug development timeline by repurposing an existing drug so I think there's a lot of interest in repurposing as opposed to starting from the beginning with a brand new molecule that no one knows anything about.

George Vradenburg: There is a question online here about how long does it take for NIH to approve the new drug. As you've gone through the timeline here, let me outline what I understand. Depending on the nature of the drug, the size of the trial, the number of sites involved, the phase one trial can be anywhere from a year to two to three years. The phase two is another two to three years. The phase three can be four to seven years depending on the population you're aiming at, and so if you really look at this as Dr. Turner indicated, this can be anywhere from a six up to 15 year process.

A repurposed drug is going to be very much at the low end of that. A prevention drug, trying to identify people who are amyloid positive but have no symptoms, will take much longer to recruit and because you have to spend a longer period of time testing what the treatment effect is, it takes a longer trial. That six to 15 years or five to 15 years, compares to about nine months for the FDA to review the actual drug assuming that it's a breakthrough drug and with respect to any new potential drug with respect to Alzheimer's, it will get as fast-tracked as the FDA can fast track it. It is not the FDA process that holds this up so much, it is how long it takes to get to the scientific evidence that you have a safe drug that's effective in whatever population you're studying and whatever stage of the disease you're studying.

We did have a question from two people who really want us to spell nilotinib more slowly so let me try. N-I-L-O-T-I-N-I-B. Roberta and Dirk, if that was slow enough, terrific. Otherwise, let us know, but we will definitely include it in the write up.

Dr. Turner: I know since this drug is already available now, it can be prescribed off-label, but we would not recommend that until we get more information about its safety and tolerability and effectiveness in individuals with Alzheimer's and Parkinson's disease. I know some people may want to rush out and ask their physician to prescribe this, but I would recommend instead looking to see what clinical trials may be available near you because these are also equally promising. There are a lot of phase three trials that are available to join, so instead of rushing out to start taking nilotinib I

would certainly look into what clinical research may be available for you to participate in. This would be much better in moving the field forward and discovering new treatments.

George Vradenburg: Mindful appropriately of your strong counsel not to take an existing cancer drug and just assume that you can take it and it will have some effect. What is the current name of the cancer drug and how do you spell it?

Dr. Turner: The other name for nilotinib is Tasigna. T-A-S-I-G-N-A. Don't ask me where they get these names from, I think they have a committee.

George Vradenburg: What would be the dosage of Tasigna that would be recommended by a doctor these days for cancer?

Dr. Turner: For cancer it's usually in the range of 400 to 600 milligrams daily, which is higher than what we're proposing for our trial.

George Vradenburg: What dosage are you using in your trial?

Dr. Turner: We're starting at 150 milligram once a day for six months, and then 300 milligrams, two pills once a day for the next six months. This is about half of the dose that is used for cancer.

George Vradenburg: We have a question online. This is from Nancy Dunbar, Nancy thank you, what are the side effects of this drug or the side effects which you're watching for in this drug?

Dr. Turner: A major side effect of concern was the EKG abnormalities or the heart rhythm abnormalities and abnormal heart rhythms. This is a major concern and this is why we're doing a lot of EKGs during the course of the trial to make sure we don't run into problems there. We'll also, of course, be screening out individuals who already have cardiac rhythm abnormalities and they will not be allowed to participate in the study. That's really the major side effect. We're not expecting to see any other significant side effects. There are the usual side effects that have been reported such as nausea and rashes and things like that. There's certainly a possibility for other side effects, but really the major one that we're concerned about is this cardiac arrhythmias.

George Vradenburg: Shelley Moore from USC has asked is there an online resource, a study website link, or other online resource that you could share?

Dr. Turner: Yes, you could look at our own website. It's memory.georgetown.edu. There's some information on there. On the front page of our website we have all of our actively recruiting studies, and then further back we have the other ongoing studies which are already fully recruited. There's

also information on the nilotinib trial if you go to clinicaltrials.gov, which is also a great website, and all of the clinical trials in the United States are registered on this government website.

There is also open access of a publication on the pilot study with Parkinson's disease, which was published in the Journal of Parkinson's Disease in 2016. There's information in there about the 11 patients with Parkinson's disease who were on nilotinib for six months and their results. That looked very promising and very exciting, and of course led to these two phase-two trials that are now ongoing. So memory.georgetown.edu and clinicaltrials.gov, and then also the Journal of Parkinson's Disease has the results of the phase one pilot.

George Vradenburg: We have a question here from Hugo Geerts. Thank you Hugo, a well-known European researcher. Will the trial have any amyloid or tau imaging readouts?

Dr. Turner: Absolutely. We are going to do spinal fluid collection at the beginning and the end so we will have amyloid and tau proteins examined. We will also do amyloid PET scan at the beginning and the end of the Alzheimer's trial. I don't think there's really any PET imaging for the Parkinson's trial because there's really no good proven ligand yet, but certainly for the Alzheimer's trial we will have proteomics of spinal fluid as well as PET imaging. We tried to include tau PET in the nilotinib trial, but we weren't successful in getting the PET ligand for the tau PET so we're just going to do amyloid PET as well as volumetric MRI, cognitive outcomes, and proteins in spinal fluid.

George Vradenburg: Joanne online asks, is someone with a pacemaker a potential participant in this trial?

Dr. Turner: That's a great question and unfortunately because almost all of our research requires MRI scans, anyone who has a freely moving metal object such as pacemakers are not allowed to participate in our studies. The other exclusion is individuals who are on blood thinners such a Coumadin are also excluded because we do a spinal fluid collection as part of the study. That unfortunately excludes quite a number of individuals who may want to participate in our studies, those who have a pacemaker and those who are on blood thinners.

George Vradenburg: A reminder to our audience for those of you who are on the phone, please press *3 if you have a question and have your question available for our staff and we can put you on the air in a few minutes and I will come back to you in a few minutes, Kathleen from Philly.
We've got a couple more questions about exclusion. A question from Romayne Jones online, would someone with Alzheimer's already taking Aricept and/or Namenda be eligible for the trial?

Dr. Turner: Yes. As I said, the first thing we do in our clinic is we make a diagnosis and we start approved medications. Then, once someone is stable on approved medications we start talking about possible research participation. We are not withholding or withdrawing any medications that are already approved that have shown to have some benefit for patients with Alzheimer's disease and

the same with Parkinson's disease as well. So there is no problem with approved medications and that's sort of expected that people will be already taking these medications.

George Vradenburg: We have two questions here from Ana online. They have to do with minority participation. These are more general questions, but I would also ask if you are targeting minority participation targets for your trial. Are there studies breaking down Alzheimer's for minority groups? And in terms of studies what percentage of participation are from minority groups? Asian, Hispanic, African American?

Dr. Turner: That's a great question. Alzheimer's affects all groups in the United States. In fact, it affects African American and Hispanic populations even more than Caucasian populations. Unfortunately, the individuals who choose to join our studies tend to be primarily very educated Caucasian populations and so our studies are typically 90 percent Caucasian and 10 percent minorities. We try our best to try to recruit minorities and increase the number because obviously if we find a treatment we want to make sure that it's a treatment for everybody and not just for Caucasians. We certainly try to boost minority recruitment in whatever ways we can. We give presentations, do advertisements. It's another one of our goals to really boost our minority recruitment to all of our clinical trials and clinical research because we need to know the risk factors and whether drugs have benefit for all populations.

George Vradenburg: This is a compliment to Dr. Turner, he's got a ten percent minority participation rate, but the average around the country is more like three percent. Probably the places of highest minority participation are Atlanta, D.C., Chicago, and large urban areas, but around the country minority participation in these clinical trials is way below what it should be and that is one of the UsAgainstAlzheimer's goals as it is with Dr. Turner.

I have got two general questions. The first is a number of people think that taking on repurposed drugs while it in theory has the great advantage of taking drugs already on the market thus safe and effective for one purpose, and therefore you can shorten the period of time to test those drugs for another indication. The downside of that is that the companies that support the much higher cost phase three studies may not have much of a patent incentive to do so since the drug has already been on the market for a period of time, and thus there's not much patent life left to justify the investment in phase three trials. I'd be curious as to how that pertains, if it does pertain, generally in your view or specifically with respect to nilotinib.

Dr. Turner: That's a great question and we certainly ran into issues that you brought up. Let me say, first of all, that the pilot with Parkinson's was entirely funded by philanthropy. There was no other source of funding for the pilot. The company was engaged and was certainly interested, but was not really interested enough to provide any support for repurposing the drug for neurodegenerative diseases. We continue to run into the same problem, even with the Alzheimer's trial. We are basically purchasing the drug from the pharmacy using the grant from the ADDF, the Alzheimer's Drug

Discovery Foundation. Again, because the company is interested but not really interested enough to provide us support for this endeavor.

The company was, however, willing to support the drug for the Parkinson's phase two and is donating the drug, which is a multimillion dollar donation to the Parkinson's trial because the pilot has already been completed and published for the Parkinson's patients. The company was certainly very generous in donating the drug for the Parkinson's trial, but not as excited or interested in the Alzheimer's trial. We certainly have run into resistance from companies in repurposing drugs as you brought up.

George Vradenburg: The other question is if this drug were released on the marketplace what kind of pricing you could justify given the fact that the drug might be on the market for another indication? Is there an inhibition just because there may not be much pricing opportunity? It obviously affects, in a sense, both industry incentives on the one side, but also affects the access to the drug by individuals.

Dr. Turner: That's true. I think the first thing the company looks at is the amount of years left in the patent life, and then the number of years that would be required to gather the data for approval for another indication and see if any investment could be recovered. But nursing homes are incredibly expensive so any drug that is effective for Alzheimer's disease and could delay or prevent nursing homes immediately becomes cost effective to the overall healthcare system and to individuals. The financial questions are very interesting and intriguing, and of course the companies are looking at this very closely and looking at different pricing if something became available, etc.

George Vradenburg: Dirk Walter asks if one is in the A4 study now, is one able to participate in one of your studies?

Dr. Turner: The A4 is for normal individuals - normal, cognitively healthy, and cognitively intact individuals. We only want you to participate in one study at a time. We don't want you to do more than one trial. Since A4 you have to be normal to enroll, then you certainly wouldn't qualify for nilotinib because nilotinib you have to have Alzheimer's to enroll.

We need a lot more volunteers for our studies so we're glad that you're volunteering and we wish we could find more people like you, but we really only want people to join one study at a time. You certainly can join one study and then when that study's completed several months later join another study so we've had several individuals who are on their third or fourth clinical trial now, but certainly not at the same time.

George Vradenburg: I have a good question here from Ashley. Is there any data available about the rates of Alzheimer's and Parkinson's in those already taking nilotinib for myeloid leukemia.

Dr. Turner: That's a great question and I don't think we have enough individuals who meet those criteria and the data is certainly not collected in any organized manner. I think we have no idea about the answer to that question.

George Vradenburg: Another great question, these are really sophisticated questions here, are there any other medicines, foods, or activities that might promote autophagy or emulate the effects of nilotinib, beyond nilotinib?

Dr. Turner: Yeah, there are several drugs that are in this class called tyrosine kinase inhibitors that all seem to promote autophagy and therefore are useful cancer drugs. There are about eight different drugs in this class that have been approved, and as I said they were certainly a breakthrough in leukemia treatment.

There's another method to promote autophagy and it's called caloric restriction. Caloric restriction means consuming only two-thirds the normal amount of calories. This also is a method of promoting autophagy. Caloric restriction, of course, works great with different animal models of Alzheimer's and Parkinson's and this was the basis for another trial that I just completed which was the Resveratrol trial. Resveratrol is also thought to be a mimic of caloric restriction and may work to also promote autophagy, but the pharmacokinetics of Resveratrol is not very good and very little gets into the brain. Almost all of it is metabolized very quickly, but this is another potential strategy that could be developed. Not just caloric restriction, which is of course very difficult to do over the long term because you're constantly hungry, but developing drugs along the lines of Resveratrol may also be another method to promote autophagy.

George Vradenburg: A couple questions from callers here. Kathleen Sliman, please put forward your question.

Question: Hi. The holistic or turmeric, have you done studies as far as that is concerned at prevention possibly or helping in any possible way?

Dr. Turner: I have personally not done studies with that but other people have. There's literature about turmeric, and its active ingredient curcumin, perhaps also being beneficial for Alzheimer's disease and it seems to have some effects in animal models and is being investigated in human studies. The problem with curcumin also is that it's a large molecule and it's difficult to get it into the brain. I think it's stuck in how do we get this molecule into the brain and hasn't really come to any effective treatment so far.

George Vradenburg: Another called, Don Carano from New Hampshire. Don, would you please go ahead and ask your question?

Question: Yes, I wonder why we don't just use the name Tasigna because I don't think anyone can spell or understand nilotinib. The drug can only be purchased as Tasigna, it's not marketed any other way.

That out of the way, there are no trials available anywhere in the world that I could find other than the Georgetown trial and you have to live in the Georgetown area to participate.

The question that I have is why the recommendation isn't for early stages of these diseases why it's certainly necessary to jump through all the hoops and get the FDA approval and do all the trials, but in the late stage people who had very good results in the 11 people that Georgetown did in the original trial two years ago, they were late stages, why wouldn't we have a recommendation that the doctors could and should, by law they can, prescribe the drug off label for the elderly who may be able to enjoy a few more years of the golden years if they don't die before? We have just one recommendation and that's not to use it and the doctors won't prescribe it because of that recommendation by the establishment. Thank you for taking my question.

Dr. Turner: That's a great comment, and the recommendation is to seek out clinical trials that are close to you. These trials are being done across the country, and as I said, the phase three ones are very large and multi-centered. Phase three means it's already been through the phase two and looks very promising and exciting, so my recommendation would be to find out what clinical trials may be available close to you for you to learn about and perhaps participate in. The phase two nilotinib, if it is successful at Georgetown for Parkinson's and Alzheimer's, in two to three years from now we may be launching a multicenter national phase three trial. Then at that point, perhaps, individuals across the country could join a nilotinib trial.

From the pilot study, it could all be a placebo effect. We certainly know that a lot of neurologic diseases have a very strong placebo effect and without the placebo you don't really know if this drug is effective or not and therefore we don't have enough evidence really to prescribe it. We certainly know that it does have some safety risks and it has a cost and side effects. If we don't know it's effective but we do know that it has risks and costs, then we don't really have enough evidence yet to prescribe it. As you say, I know that there are some people who are looking for this drug and want to try the drug and they're getting the drug off label. I know it's happening, but it's not something that we recommend.

George Vradenburg: I've got to thank you, Dr. Turner. You are crisp, clear, and obviously quite thoughtful and really on top of your game. I really want to thank you for spending some time with us today. I acknowledge there are many questions we couldn't get to today. This was a particularly voluble group, at least online, who asked a lot of great questions.

Just a couple program updates. Tonight on PBS at 10pm eastern, PBS is going to air a national documentary called Alzheimer's: Every Minute Counts. It will feature one of our advocates, an

UsAgainstAlzheimer's advocate, named Daisy Duarte in that film who's a young lady who's taking care of her mother and also herself has the familial mutation for Alzheimer's. It's a compelling story, but she is one of several personal stories. Yours truly is actually in the product as well so this a little conflict of interest but I'm going to be in the program.

The other program note, our next call is February 23 at 3pm Eastern with Dr. Nathan Rose from the University of Notre Dame. Dr. Rose has a fascinating series of research in which he believes that his MRI technology can actually watch memories being formed and then forgotten. He is going to describe this research and the fascinating implications, if his work is validated, what the implications are for what we might do to address the Alzheimer's crisis. Please, if you'd like to be registered for that call, click here. We hope you're able to join us next month.

If you haven't joined UsAgainstAlzheimer's already, please go to www.usagainstalzheimers.org and sign up. We'll send you not just a recap of this call and invitations to future calls, but important updates and simple ways that you can actually get engaged and affect things here in Washington. As my wife Trish says, the driver in my life, numbers count. Please encourage your friends and family to join us. The more people we have the more attention we'll get from Congress, the media, and from industry.

Thank you to everyone on the phone or online for participating in this Alzheimer's Talks. In a couple of weeks, we'll have a copy of the recording and a transcript on our website for you to share with friends. If you wish to leave us a message, please stay on the line. We'd love to hear your thoughts on today's call, and also any suggestions you have about topics or individuals that you'd like to have featured on upcoming calls.

Thank you for joining us today, thank you Dr. Scott Turner of Georgetown. I encourage anyone on the phone who lives in the Washington D.C. area and who believes they might qualify for either his Alzheimer's or Parkinson's trial to please give Georgetown a call on the online resources he indicated earlier.

We appreciate your time and appreciate your participation and engagement in this fight to put a stake through the heart of this ugly disease. Thank you very much and have a great day.

Dr. Turner: Thank you.