Welcome
Maria Carrillo – Alzheimer’s Association

Maria started the meeting stating it has been their pleasure at the Alzheimer’s Association to help the WW-ADNI effort come together and give space and time to share ideas and thoughts and to potentially get to know one another and what each other is doing at their respective clinics. Ultimately the goal is that anything that happens at a particular center is magnified by moving past their country borders. Maria states she believes this is happening as she is watching the meeting grow over the years. She congratulated everyone and thanked them for their attendance. Maria asked Neil Buckholts from the National Institute on Aging to start the discussion and for Holly Soares from the Industry Scientific Advisory Board of ADNI to follow him.

Neil Buckholtz – National Institute on Aging

Neil began speaking about the beginning of ADNI. He stated there has always been industry participation in the public, academic and private sector which was crucial to the success of ADNI. The idea of a public/private partnership has been critical to the success of ADNI and he thinks it will be as they try to go forwarding thinking about ADNI II which will be covered later. He stated that the exciting thing for him was seeing the public database being used. From the very beginning this was conceptualized as a database that would be open for everyone without any particular access. Neil stated several neurological and non-neurological groups are trying to devise ways to use the ADNI model to do the same thing for their groups which has been done for the Alzheimer’s group. Neil thanked everyone especially the WW-ADNI; he noted there are various other databases out there and how exciting it would be to get all of the databases together. Neil stated this would be a tremendous accomplishment with more subjects in Alzheimer’s disease who have had all of these evaluations then has ever been accomplished before. He felt this could be one of the goals for the future to try to get all of the databases together so there will be a greater amount of data available for people to access. Neil thanked everyone who has been involved with
ADNI in the past and everyone who is considering working with ADNI; and to the international groups who are thinking about setting up these kinds of studies because he feels it is a very powerful way to develop some progress in AD and utilized this to look the progression and diagnosis and of AD and eventually to be able to use these imaging modalities in clinical trials. The bottom line is to get therapies out to individuals and families who are suffering from this disease. Neil stated that through ADNI they will be able to facilitate these kinds of therapies for Alzheimer’s disease. He closed by thanking everyone there for their accomplishments and looking forward to the future.

Holly Soares – Chair ADNI ISAB (Pfizer)
Holly stated there is a worldwide presence which created a worldwide community and a greater appreciation for understanding of early forms of Alzheimer’s disease so now they are having a meaningful dialogue about prevention. She thanked all of the participants of ADNI as they have all in some way contributed. Holly closed by introducing Mike Weiner

ADNI Data Update
Mike Weiner, UCSF – Overview
Mike started by thanking Maria Carrillo and the Alzheimer’s Association for sponsoring this meeting every year as it gives everyone a chance to meet and speak about their research and progress. He went on to thank the Japan-ADNI group for their participation. Mike stated they are doing marvelous work and there is nowhere for them to go except on to bigger and greater things and they will be using more technology. Mike stated it is critical that they give a warm welcome and share technology with investigators from China who have the same interested as you do.

Mike stated the ADNI I grant was funded 5 years ago in October and it is coming to the end of the fifth year of funding. They are going into a No-Cost Funding. From October 1, 2009 to October 1, 2010 ADNI will continue to use the funds originally awarded for the one year. September 2008 marked the end of the one year follow-up of the subjects in the trial. In a year from now, September 2010, subjects will be completing their 3 year follow up. In summary, the way the ADNI data is looking now you can image how the data can be used in the following ways: you can look at outcome measures, you can look at rates of change using clinical and cognitive measures, MRI measures, and PIB Pet measures. Furthermore, they are using some of the data, CSF as an example, as predictors because some information appears to have value as a predictors and so far they are not see changes in the data as an outcome but it is extremely useful as a predictor as it appears to identify subjects who are not demented but have Alzheimer’s pathology in their brain. Currently in ADNI, the image analysis lab has been analyzing all of the data from the 2 year follow up and the bio stat core now has the data and is working over the next couple of months on completing a very large complicated set of analyses. The analyses will form the future set of hypotheses for the ADNI renewal grant which is due November 1 and they need to be writing the grant in August and September. ADNI applied for a GO (General Opportunities) Grant. These are funds that come from the stimulus package from the government and appropriated to the NIH. Mike stated they are applying for $24 million and they don’t know if they will receive it. He stated Neil Buchholtz told him the grants are going to be reviewed at the end of July and early August so by the end of summer they should if they are going to get the grant. Mike stated this will have a big impact on how they write the renewal grant. The GO grant had 3 major funding requests: 1) to enroll an early MCI cohort (people with symptoms with very mild impairment but who do not meet the criteria for the more severe form of MCI that they have currently been using in ADNI); 2) they put in to do Amyloid imaging with F18AD45 on all of the new subjects to be enrolled (that would be the early MCIs) as well as current MCIs and controls and current controls that is ready in ADNI – funds were requested to follow the subjects for 2 years; 3) to do a lot of data analysis, statistics and image processing. If the GO grant is not funded then the $60 million that is available for ADNI II will be very, very tight if they are going to be doing Amyloid imaging and enrolling early MCIs and continue MCIs and controls from ADNI I and also enrolling new control, new late MCI and new AD into ADNI II. He stated the hope has been with ADNI II that they
will continue with the current subjects (about 530 subjects) into the renewal and they would also enroll early MCIs as a new population and some new controls and some new late MCIs and 100 patients with Dementia as well. The ADNI II would have 900+ subjects and they would Amyloid imaging on all of them; they would absolutely like to longitudinal Amyloid imaging on all of them as well because they want to do a baseline to see how baseline predicts future decline but then they would also like to get another time point to see what the naturalist change of Amyloid imaging shows. So these are ambitious goals to reach those targets if the GO grant is funded. Even if it is not funded they can still do a lot with the $60 million and the grant renewed. A successful renewal of the ADNI grant requires 2 things: 1) cooperation from industry to provide 1/3 of the funding. The NIH has indicated that $40 million would be available if the group submitted an application and it was successfully reviewed and then it would also have to have a grant that gets a good score on peer review. It definitely is not a given thing that whatever is put it will be funded. The people who are reviewing us would outside, standard peer review for NIH and the group would have to sweat it to get a good grant in but Mike is sure they will be able to do it. Mike stated Bill Jagust will probably cover the issue of types of ligands available for Amyloid imaging and what they would be using in the ADNI grant. For the GO grant they stated they would be using the Avid compound 45 because the GO grant if funded would probably begin September 1 through October 1, 2009 and they needed to have a company to agree to provide F18 Amyloid imaging at the vast majority of the sites across the county and Avid has assured them they can provide it. They have negotiated a budget with Avid and wrote it in the GO grant. If the GO grant is funded and they do all of the imaging with the AD45 another question will be at the ADNI renewal, how do they accommodate other companies that have F18 Amyloid ligands and how do you deal with the issue of long-term follow up of patients with these grants; perhaps there will be questions about this and perhaps Bill will want to cover it. Mike stated regarding what will be in the renewal grant they are asked what will the questions be, what will the hypothesis be, exactly what will the grant be focused on. Mike said he thinks the best answer he can give you today is that it depends on bunch of different things. What are the result of the biostatistical analysis that is ongoing now that should be completed by the end of the summer or September. Without question some of the major hypotheses that will be addressed in the ADNI renewal grant will be replication of findings that came out of the original ADNI. In the original ADNI, it was written as an exploratory grant. He stated that in the original ADNI the group did not have a lot of pre-specified hypotheses there has been a lot of data exploration and different people have been looking at the data in different ways and writing different kinds of papers. Mike stated they wanted to look at the various outcomes and predictors at the various stages of progression of the disease. Another big question that is critical to look at and is repeatedly discussed is Amyloid imaging and lumbar puncture in CSF getting to obtain levels of Abeta and CSF. There will be completely new hypotheses because they will be enrolling in this early MCI population. In ADNI they do not have experience with them and if you review the literature it’s a little mixed about the available data in the biomarkers of early MCI. There are a lot of data biomarkers in MCI and a lot of data biomarkers on controls but not that much on the bridge population. The other thing they need to do know is gather all of the publications from people outside of ADNI and all of the abstracts outside of ADNI. Mike stated he is currently working on this. Mike hoped the companies that are working with the ADNI database would have a little more communication with them and tell the group what they have found and what results they have had. Mike stated they have not had a lot of dialogue like that and that it would be very helpful because they want to get the most out of the dataset so they can write the best application.

Paul Aisen/Ron Petersen – Clinical Core
Ron stated he wanted to take a couple of minutes to talk about the clinical core and what it means to ADNI. He stated it is the nexus of the entire grant; it is not where the action is but it is a vital component of whom they are studying and what kinds of subjects they are going to be looking at. The progression rate for that group from MCI to AD was about 16% per year and ADNI the first year plus is about 16-17% per year so it appears that this is doable but again the sites was the ones who were able to accomplish this. Also, the dropout rate is staying low around 6-7% per year and they had projected a
10% dropout rate so the sites are really doing the work of recruiting the right cohort of subjects and keeping them in the study to allow us to test the various hypotheses that Mike alluded to. The primary interest is moving the threshold back earlier and earlier in this disease process and trying to pick up people in the symptomatic and ultimately the pre-symptomatic stage. In doing so, they are going to try to recruit a cohort of early MCI subjects in ADNI II and this is going to take a little imagination on their part in terms of trying to define this group and they have put out some clinical characteristics that they think they will be capturing a more mild group but as they do they are going to increase their sensitivity to pick up new cases but probably sacrifice some specificity with respect to clinical outcomes of these subjects. Hence the neuroimaging and chemical biomarkers will help us stratify that group of early, early patients with memory impairments by the biomarkers and say which ones are going to go on to develop AD. That is the big picture of ADNI II and Ron thinks that is where it is headed unless they put in the GO grant and will put forward into the ADNI II application. Because of industry's interest in this area there is likely to be therapeutic trials that are also going to be encroaching on this area appropriately it will be a challenge for us in terms of recruitment because you can’t participate in both so they are going to have to make it sufficiently attractive that they are adding information to the field that will enhance their recruitment of these subjects. Finally, Ron mentioned his role on the Medical and Scientific Advisory Committee of the Alzheimer’s Association, the Association has been critical in terms of the worldwide ADNI approach. The Association has provided some stimulus funds for European ADNI and he thinks that is moving forward well, as well as Australian ADNI with trying to integrate the database into general US and NA ADNI approach. Ron stated they have been working very closely with Takeshi and colleagues in Japan so that Japanese ADNI and US ADNI are really very similar in respect to certain features. So, hopefully as has been suggested they will be able to bring all of these ADNIs together with a lot of commonality and increase their size and power to detect some real signals here.

Bill Jagust – PET Core
Bill stated he has been very fortunate to work with a group of people who have been very collaborative and the sites have been tremendously collaborative. Through it all they have been able to give up the individual approaches to how they collect data and do it all the same way. ADNI speaks loudly; it is a multi-center study and it shows if you can do this across multiple centers with multiple PET scanners and multiple diagnosticians calling people different diseases than it really has some weight. It speaks loudly and with one voice and Bill feels this has been a great accomplishment of ADNI that doesn’t get recognized. He ended with the issue of Amyloid imaging and the future and as Mike told the group the two things about the direction of ADNI II that Bill feels is exciting are the idea of an early MCI group and Amyloid imaging. There are currently four F18 Amyloid imaging ligands that could be used and Advid has been very helpful with getting the ligands out to multiple sites around the U.S. They have a distribution network, a phase 3 study and an IND so the group has linked up with them for the GO grant. There is a twice monthly call with PET and most of the companies involved, a lot of which were involved with the Amyloid imaging, have been on the call. The whole approach for Amyloid imaging in ADNI II vis-a-vis Amyloid imaging is not a closed door. They need to keep talking and do what is best to get the grant funded as Mike has said. Bill stated everyone knows five years from now there will be multiple imaging agents out and everyone will be asking how are they different, how are they the same and so forth. This is an area that has to be discussed collaboratively.

Mike Donohue – Data
Mike started by saying he will be comparing a time to event analysis, a time to conversion from MCI to AD to a linear effects analysis of serial standard outcomes and along the way they will be considering Amyloid disregulation – enriching the sample that way and confirming what has been seen before with increased efficiency by ADNI and baseline covariate. Some issues with the time to conversion endpoint; it is practically difficult to implement, there is subjectivity, there is difficulty having clinicians reach a consensus about whether a patient has converted or not, some might argue it is an artificial distinction between MCI and mild AD and there is certainly a lot of variability with subjects converting and
reverting over time. In trials in the past, proportional hazard assumptions have failed when the Cox model has been planned and to begin with the standard Cox model is not appropriate for a planned visit schedule. So when they observe a schedule at month 18 you really only know the conversion occurred between month 12 and 18. They don’t know in fact that month 18 is the time of the event. One of the underlying assumptions of the Cox model is that the hazard function is proportional for each subject and conditional on the covariate. Technically, the assumption allows you to simplify the likelihood function; it allows for some nice cancellation of likelihood function and it makes the likelihood function easier to maximize.

Neil Bucholtz – WW-ADNI Renewal

Neil stated that this was an opportunity for industry attendees to make any comments or ask any questions of the ADNI investigators regarding the competing renewal. At this period in ADNI, coming in with the data that has been developed already, the hypotheses are going to be critical in terms of a successful period review. Neil states that if any of the group, especially those from industry, have questions about the initial hypothesis, it will be revised as they go forward and get more data.

Holly Soares asked the first question and started by thanking the ADNI PIs for being very responsive to the ADNI ISAB questions and request but there has been a lot of recent discussion around hypothesis driven questions from ISAB. In the beginning ADNI was about looking at change over time and longitudinal assessment and a lot of the analysis is based on that but now a lot of us are focusing their eyes on prediction, can they come up with markers that will identify that early AD population. Although they are looking at biomarkers to look at it in an exploratory way, they haven’t power the study based on looking at the predictions. So if they can’t get it in ADNI II is there a way they can synergize activities with WW-ADNI, maybe for some reason they can’t get the power because of financial reasons but is there; she would really like to hear from their WW-ADNI partners in terms of using some of these biomarkers like imaging and CSF to ask the question or hypothesis is these biomarkers predictive of being at risk for developing Dementia or Alzheimer’s?

Neil responded that from an administrative point of view from NIH it is not so easy to do that. It is going to have to be a self-contained application but certainly that is their hope that this data will be used to answer the kinds of questions you have and he turned it over to Paul.

Paul stated these are the types of hypotheses that need to be written in the ADNI II application. He thinks they can address the predictive value of various biomarkers by themselves and using ADNI I data and using ADNI II they can both confirm that the initial exploratory assessments are correct and extend them to other populations; specifically to the early MCI population and in addition he thinks a big goal of ADNI II should be to go even further with the public sharing of data to facilitate combining ADNI data with external datasets, both international ADNI datasets and commercial datasets and academic datasets to give us the best opportunity to learn the most about the data and how generalizable it is.

Eric Siemers (Lilly) made a comment/question. He stated a couple of years ago he had the opportunity to chair the ISAB and most recently he had an opportunity at his day job to start for pivotal trials in 30 countries at over 300 sites all over the world and stated as you go out to places all over the world and you tell them that in your trial you may not be doing things that are exactly like ADNI but in an ADNI like way that really gains some traction and he thinks the real intent of ADNI was to develop the methodology and was not hypothesis driven it was really to develop the methodology in multi-center studies and to be descriptive. He continued stating that as you look forward to ADNI II you ask can this be done in a multi-center trials and the answer is yes and they have a lot of methodology worked out but in ADNI II they would like to be more hypothesis driven and ask some biologically relevant questions and he thinks the point that is of interest to people in industry is this really patient population and that is where it is important to replicate some of the ADNI findings to extend ADNI follow up and kind of consider the secondary outcome measures. He thinks for the group it is the early MCI symptomatic group that
becomes of interest and asked the international contingent if they felt it has the same traction as they think it does.

Comment on importance of early outside of the US: the importance of the early group is really essential. They are looking at now patients who have underlying AD pathology in the earliest detectable patient they can treat. One of the big things on their wish list for ADNI II is can they actually drill down to what the predictive value of all of the particular markers are to determine how they best select the patients, he believes they are at the point where they can begin to conceptualize the study. How do they operationalize it, how do they turn the biomarkers into statistically relevant, positive, predictive value studies, how do they find these patients with a degree of statistical certitude, and what happens to those patients over a period of time. He thinks they are close and ADNI I has exceeded all expectations in that area and ADNI II will move them closer.

Andy Simmons – UK Efforts
Andy started by stating he was speaking on behalf of a European consortium. He had four points to review for the presentation. He was covering a little bit about peripheral biomarker discovery, touching on some multi-variate analyses they have done and a final slide touching on where they are going with their grant. AddNeuromed the study he is representing had scanned about 400 people and the pilot E-ADNI had about 60 or so. They have agreed to work together in Europe and to harmonize their efforts as best as they can. The AddNeuromed has 2 arms: pre-clinical and clinical. He is only going to cover the human imaging arm and their approach has been to use MRI as a tool as to focus on proteomics, lipidomics, genomics and metabolomics. They are interested in diagnostic markers, progression markers and surrogate markers using trials. He focused on the proto mix which he believes is their most advanced effort. They have recruited over 700 people into the study, of whom over half about 400 or so, have had a MRI. Their study uses a baseline of three months and a one year follow up with clinical assessments and blood being taken every three months. They have used 3 approaches to look at proteomics in MRI: a case controlled study using 2DGE with mass spec, a severity markers discovery study using imaging correlation and final one a progression marker study using proteomics. Their aim was to get together a panel of proteins measured from blood plasma and to see what they can do in an unbiased manner. They then went on to use MRS measures to try and see if there was a correlations with the 2 measures: weak but sufficient correlations were found. He wanted to emphasize that they were not trying to say that any one of the proteins is going to be a killer application but it is more getting a panel together that reflects change. They used a discovery phase of about 70 people using MRI looking both at hippocampal volume and rate of decline to try and pick out protein front runners that might be an indicator of Alzheimer’s disease. They went on to validate this in a larger sample of about 700 people. Finally, they did some collaborative work with NIH Intramural study, the Boston Longitudinal Study of Aging, using blood samples acquired 10 years before PET/PIB scans. Out of all of the three phases they were able to show the clustering is a plasma biomarker of severity progression and pathology. They have been using a new approach, an approach using an intelligent network which basically minds public domain data sources looking for association between candidate proteins. The number one hypothesis that was generated by this intelligence network is that CRP should be a potential biomarker for AD. They found there was no significant association with baseline CRP but there was a highly significant correlation with baseline CRP and rate of brain atrophy. He felt it was quite interesting that you could get a prediction from an intelligence network tested using one year follow up data from MRI and get something that turned out to be positive. In terms of following up, they are looking for a proposal AddNeuromed II. They have spoken with colleagues and Europe and are looking for various funding streams. Joint analyses with ADNI is high on their list, and they are talking to Andy Sakin during the week about some of the genomics, they are looking at pooling the data and what more power can they get by combining their imaging and their GWAS and ADNI’s imaging and GWAS.

Giovanni Frisoni – NeurGrid Europe
Giovanni thanked Maria for giving him the opportunity to give an update. There’s a cross sectional, only cross sectional issued in Italy – they can call it Italian ADNI. There is an initiative by Peter Jelle Visser on CSF markers, carried out in close cooperation with Les Shaw and John Trojanowski. He gave an update about the NeuGrid, European Commission funded project, and an update on the ADNI-related effort regarding the harmonization of the hippocampal tracing, partly funded by Lilly and Wyeth, which he acknowledged.

Giovanni discussed an initiative closest to ADNI that he knows of. It’s a newly funded effort. The title is one that you can read yourself; the acronym is PHARMACOG; it’s a 22 million Euros public/private partnership. It’s coordinated by EFPIA, the European Federation of Pharma Companies, and specifically by GSK. Together they have an academic partner, the University of Marseille, in France. The aim is to develop new markers, homologous in animals and humans. So the key challenge here will be to work in the clinical groups, they need to work in close cooperation with people working on animals.

Within the 22 million grant there’s a work package, specifically devoted to human studies that Giovanni is leading whose design is very similar to the ADNI. There’s a number of companies in the Consortium which will develop new biomarkers, mainly focusing on plasma and serum biomarkers. And this is the clinical centers that will take part in the human studies. Half of these are part of the European Alzheimer’s Disease Consortium.

A short update on NeuGrid. Let me just remind you that NeuGrid started as a European funded project for 2.7 million Euros. It started as the repository for European ADNI; it evolved into a computational infrastructure. Presently, the architecture is made of five centers: one grid coordination center in France, one data coordination center in Zurich, and three computational centers in Brescia, Stockholm and Amsterdam. The architecture of the infrastructure is in place. The aim of the infrastructure is to provide computational power for computer-hungry applications. For example, cortical thickness extraction or independent component analysis of resting state of MRI data. Or think of any computer-hungry application that you can think of. The architecture is in place, they have run a first test of the algorithm running on the networks; they will do a massive data challenge on the whole grid infrastructure in September by extracting the cortical thickness of the whole ADNI dataset.

Giovanni stated the novelty is that a few months back they have submitted a bid to the European Commission for international cooperation. The idea was to promote interoperability of the new computational infrastructure with two other computational infrastructures: one is the LONI that you may have heard of, and the other one is a newly born, which is an infrastructure that is presently being developed in Canada, C-Brain by Alan Evans at the MNI. This project is called OutGrid because it’s going outside Europe - not very creative perhaps. It’s a half million Euro project. So it’s not big, but the aim is not to carry out the interoperability but to promote funding of a large effort that will develop interoperability.

Giovanni gave an update of the E-ADC and ADNI effort for the harmonization on hippocampal tracing. The design of the project is that they will survey all the available different protocols for the manual tracing of the hippocampus. A Delphi panel will come out with one single harmonized protocol and with the harmonized protocol, they will build probabilistic maps of the hippocampus that will be used as a golden standard for a number of purposes. This is the working group, there are E-ADC centers, there are U.S. ADNI centers and other centers and the number of useful boards.

Giovanni stated they have reviewed the 10 different literature protocols focusing on the inconsistencies of anatomical landmarks. They have checked their understanding of the different protocols with 7 out of 10
authors, protocol authors. Three conferences will be scheduled in September. What they will do in the future, an expert panel will agree on a harmonized protocol, as he said, through a Delphi procedure.

Lastly, Giovanni took the opportunity to make some advertising here. The Neurobiology of Aging where he serves as the imaging section editor has launched an initiative for a special issue on ADNI studies. Mike Weiner is their very welcome guest editor. The manuscripts are expected to reach us by January 31st and the expected publication of the issue is July 2010, right after ICAD. He thanked everyone for their attention.

Maria introduced Dr. Takeshi Iwatsubo but first she took the opportunity to congratulate him on his progress with J-ADNI, which is an effort that is very homologous to the North American ADNI effort. She stated he’s going to give an update and hopefully also a brief discussion on a potential meeting that they’ll have in Sendai, Japan in November for Worldwide ADNI. Thank you.

Takeshi Iwatsubo – J-ADNI
Takeshi thanked Maria and stated he wanted to briefly summarize their progress in the Japanese ADNI. It’s just one year since they started their initial enrollment of the patients, and now their study is a 5-year study and now 8 clinical sites in Japan are expected to participate. Already 26 or 28 are starting to recruit. Their goal is to recruit 600 cases in total, with amnesic MCI, 300 and early AD normal control, 150. They’re also collecting FDG-PET and amyloid PET, and almost a half of their clinical sites are capable of doing some type of amyloid PET. Also they collect blood samples and then genotyping APOE and conducting as a genome-wide survey. They are trying to take as many CSF samples as possible. What they have been doing so intensively is to develop a clinical, about the reason Japanese version has the highest compatibility with the Western version.

So far they have recruited 160 individuals, and almost half were normal individuals, 50 amnesic, late amnesic MCI, and one AD have been recruited. One problem is that when they’re having a rate of high exclusion rate of late MCI cases, and this is due to the inclusion of relatively mild MCI basic clinicians. So now they have 1,000 and are now recruiting late (unclear) cases.

So this is demographics and among the 120 screened initial cases, as for age, it ranges very similar to the United States. The percent of females is a bit higher compared to the United States and probably somewhat more than half of the participants are females. Mean education year is about 13 years. This is a bit lower than in the United States, but probably this may reflect their population participating in the clinical trial and this is APOE-4 rate of the initial 100 cases that Professor Kwanu has tested. It was very striking that APOE, a positive late in Alzheimer's Disease, was 6%-8% and for amnesic MCI this APOE rate was almost the same. And then in very sharp contrast, (unclear) rate in the normal controls was very low. So this may suggest that Japanese clinicians recruit in prodromal Alzheimer’s in a very, very quick fashion.

Summaries: enrollment started at a good pace and they have recruited 163 in less than one year, but it’s a long way to the goal and their goal is 600 cases. Then they have to emphasize that the burden for individual sizes is slightly heavier as in United States, but they have to encourage the clinical size. They have seen the optimal compatibility in the clinical and psychological tests.

An Worldwide ADNI meeting that has been scheduled on November 22-23 this year in Sendai. Professor Hiro Arary is the President of the Japanese Dementia Society. For a year now they’re scheduling the worldwide meeting starting from the afternoon of the 22nd Sunday and lasting past noon of the 23rd. This is in Matsushima area, very close to the Sendai area. This is Chusonji also, because they’re planning an excursion for the participants to this area. That is just 30 minutes from Sendai downtown.
So the last thing they have to discuss is one possible plan agenda of the meeting. As you see, this is divided by countries, U.S. ADNI or Japanese ADNI and there are some others. This was the original plan, but they have discussed this with Mike Weiner, Bill Thies and Maria Carrillo and they’ve come to the conclusion that they may have to emphasize a worldwide ADNI opportunity to mix up everything together, to maximize the harmonization.

Holly stated she would like to see maybe some more from their Asian participants, from Dr. Juang, who is here today and they’re going to hear a little bit more about China ADNI because she think that’s very important. And if there are any other European initiatives that they might not know about, that they’ve heard rumors of, that would also be very nice if they can include that.

Dr. Iwatsubo said they are now considering discussing addition of the Chinese folks and from UK. As soon as this meeting is over, they will start the preparation for the registration and they will finalize the agenda. Thank you very much.

Maria thanked Takashi and invited Chris Row and Cassandra Cerque to give us a talk and a little update on ABLE and what they at the Alzheimer’s Association egotistically like to call A-ADNI because they helped fund it.

Chris Row and Cassandra Cerque – ABLE (A-ADNI)

Chris starting by saying he is representing the Australian Imaging Biomarkers and Lifestyle Flagship Study of Aging, also known as ABLE. It’s sponsored by the CSIR, which is an Australian government research organization, and it involves a number of academic institutions from around Australia. There principally is a two-city study in Perth and in Melbourne. So it’s a multi-modal study. They’re using extensive cognitive evaluation, blood biomarkers are being collected in all participants, genomic analysis is being undertaken, demographic and lifestyle data is being collected, PIB imaging and MRI is being performed in 25% of the cohort. This is the cohort. The enrollment was completed, so there are 1,112 patients in the study of which 287 have had imaging. They did initially reclassify - you’ll notice that most of the movement in MCI, 20 went to normal and 46 of supposedly healthy on neuro-site testing were re-classified as MCI. They had a few ADs that went backwards.

The true ADNI study itself is halfway through the 18-month follow-up. So 95% retention rate at 18-month follow-up so far with over 800 people have had their 18-month cognitive re-evaluation and blood sampling. The imaging cohort, which is what I’m basically going to talk about today is the area that’s the most developed and which they have the most information on: 177 healthy controls, 57 MCI’s, and 53 ADs, they’re aged in the early to mid ’70s. It’s an enriched sample, so the APOE-4 percentage is quite high. They deliberately channeled APOE-4 positive individuals into this study because they wanted to have a higher chance of finding changes with time. So they went for the higher risk, healthy controls. There was also a bit of channeling of subjective memory complainers, also into the healthy control group. So remember that these results refer to an enriched healthy control sample.

Conversion rate is very interesting – 67% of their PIB positive MCI’s have proceeded to Alzheimer’s disease in two years; 22% of their PIB negative MCI’s have progressed to other dementias, basically DLD, FTD and vascular dementia. And you’d expect that because it’s quite logical that non-Alzheimer’s dementia will also go through an MCI phase.

In the healthy controls they’ve got a surprisingly high proportion of patients who have developed objective cognitive impairment, so their memory scores or their cognitive scores have declined to below 1.5 standard deviations below the mean so they qualify for a diagnosis of MCI. In a few cases they actually developed Alzheimer’s disease. So it’s 26% at 3 years so far versus 2% - this is one person who’s developed non-amnesic MCI but lacks the PIB negatives.
In their hands, now remember this is including some non-amnesic MCI patients, so it’s a mixture of the Austin and the ABLE data, the predictive accuracy for PIB to develop Alzheimer’s disease at 2 years is 82%.

Maria thanked Chris and introduced two new faces for the worldwide ADNI collaborators. First, she introduced Dr. Zhengxin Zhang. She stated they all should have received an overview of what she has attempted with Mike Weiner’s help, to put together a short bio of what’s happening at least that they know of in China. They know that this is not complete, but this as much as they know at this point, as much as they’ve managed to collect in terms of efforts that are related to biomarker and imaging efforts that are going on in China. Dr. Zhang’s is a very knowledgeable epidemiologist. She works at Peking Union Medical College Hospital and she is currently working on a biomarker effort with over 1,000 patients. So Dr. Juang is going to give us a very brief introduction on her initiative. Thank you, Dr. Zhang. Welcome.

Zhengxin Zhang – Peking Union Medical College Hospital, Peking

Dr. Zhang began by introducing their hospital’s work. The basic of information – their hospital was established in 1921 by Rockefeller Foundation

They have very big disease population and also from this study they establish a national network for research since 1997. The reason today government pays attention to Alzheimer’s dementia so give some support, so they did the study for research on early diagnosis and the treatment for dementia funded by the Chinese Minister for Science & Technology from 2006 to 2010. They found they want to find more sensitive to screen the case and early to detect the patients. There is a study is to detect dementia in patients with Parkinson’s Disease in the four regions. There is seven cities, and they can spread the four regions.

They also developed some new biomarkers like magnesium. The magnesium in spinal fluid in blood, in urine, and this one, the pilot study will complete this month. Also they did the magnesium in the brain but this is not successful because the magnesium is not stable. Also, to improve the measurements for the MRI of hippocampus so Pfizer supported a study they started in China.

Maria thanked Dr. Zhengxin Zhang and introduced Dr. Jian-Ping Jia who is the dean of the Neurological Institute of Capital Medical University and Xuan Wu Hospital in Beijing, China, also heading a longitudinal effort to MMCI.

Jianping Jia – Capital medical University, Beijing

Jianping stated he is very happy to be here to enjoy the ADNI results. He has learned a lot and he would like to take several minutes to introduce the China MCI and their longitudinal study.

Not many people know something is happening in China for Alzheimer’s Disease. Two years ago the national key technology program, during the 5-year period plan funded a big program, big project named China Cognitive Impairment Longitudinal Study. He is the PI of this study. He the director of the neurology department of Xuan Wu Hospital in Beijing and the chairman of China Neurology Association. This study is to estimate the prevalence of mild cognitive impairment, dementia and some major sub-types among elderly people in China, and to determine the risk and the protective factor for MCI and Alzheimer’s Disease. Also, they are going to explore the progression of MCI. How does MCI progressively develop Alzheimer’s Disease and why? They are also going to identify what are the predictors for the MCI. They want to find the biomarkers for MCI and Alzheimer’s Disease. For the biomarkers they make a big effort for the (unclear) testing and the neuroimaging and the genetic analysis.
This study from 2008 in Beijing, just before the project started they had a very careful and strict training for this. They collect the more than 70 persons or sub-investigators in Beijing, just give three days training including how to ask the patient their medical history, how to do the psychological evaluation.

Dr Jia briefly introduced a big project for China. This is named the Mild Cognitive Impairment and Dementia Longitudinal Study in China. As you know, China is a very big country with 1.4 billion people. With the people aging the dementia and MCI are getting more and more than before. They need to freeze this factor. They need to do some work for treatment and diagnosis of MCI and Alzheimer's Disease. They know they are behind, but I am sure they can come up with. Thank you very much.

Maria thanked Dr. Jia and Dr. Juang, for those presentations. She thought it would give the group a flavor of what is happening in China. It's a very big country. They’re just starting to find out what’s going on and make it public so that all of their worldwide collaborators are aware of what’s happening. They will continue these efforts, so look forward to Sendai, Japan.

Holly wanted to thank all the presenters for presenting their ADNI initiatives. She does want to make a comment. There are a lot of global studies in Alzheimer's disease. Although they call them ADNI, they’re not that similar if you really look at the study design, but the questions that are being asked are very similar.

The last thing she want to say is thank you to Maria for all the work she did in organizing these worldwide ADNI initiatives. They would not have been sitting here together without Maria and the Alzheimer’s Association, and David Lee from the Foundation for the NIH for pulling this all together.