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**HOUSE COMMITTEE ON FOREIGN AFFAIRS**  
Subcommittee on Africa, Global Health, Global Human Rights, and International  
Organizations  
259A Ford House Office Building  
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**The Global Challenge of Alzheimer's: The G-8 Dementia Summit and Beyond**  
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Good morning ladies and gentlemen.

Thank you Chairman Smith, Ranking Member Bass and other members of the Committee. I am Dr. Andrea Pfeifer, the CEO of AC Immune, a biopharmaceutical company based in Switzerland developing drugs against Alzheimer's disease. Founded in 2003, AC Immune takes pride in the discovery of Crenezumab, which is being developed by Genentech with support from NIH for the first ever preventive clinical trial in Colombia and the US. AC Immune has three clinical trial programs, four preclinical and a diagnostic program. I am honored to be invited today to address the members of the Committee on Foreign Affairs as you consider potential policies for discussion at the upcoming G8 Dementia Summit in London.

I have the honor to serve alongside my peers in the Global CEO Initiative on AD. My passion as a scientist to find a therapy to mitigate the medical effects of this terrible disease is matched by my determination to engage with key policymakers such as yourselves to pull together all the key elements of a Global Action Plan similar to that the world established 30 years ago when faced with the HIV/AIDS epidemic. In my view, the challenges of AD today are on the same scale, if not greater.

Let me start the session with some hard basic facts on AD:

- AD is an irreversible degeneration of the brain that causes a loss of memory, cognition, personality and other functions that eventually lead to death.
- AD is not a normal part of aging but its occurrence correlates with aging
- There is no cure.
- According to the World Health Organization and Alzheimer's Disease International 2012 Dementia Report, it is estimated that there were 35.6 million people with dementia, including Alzheimer's disease, worldwide in 2010. This number is projected to nearly double every 20 years, increasing to 65.7 million in 2030 and 115.4 million in 2050.<sup>1</sup>
- With an ageing population, the prevalence of AD is estimated to continue to grow across Europe at about the same pace as in the US.
- Several countries, including France, Australia and England, have specific plans in place to address dementia, including Alzheimer's disease.<sup>1</sup>

### **RESEARCH AND DEVELOPMENT CHALLENGES:**

As a researcher and a CEO, my specific role today is to share with you some challenges of the research and development in Alzheimer's disease. Even more than a century after it was first observed, today we still do not know the exact causes of the disease and the exact molecular basis. We do know that AD is characterized by the loss of neurons and synapses which translates into loss of brain volume and atrophy of certain regions of the brain. We also know that two proteins – Beta-amyloid and Tau – are shown to be ultimately involved in the disease process.

The goal of the research is to find a total cure. Alzheimer's disease (AD) might be treated with symptomatic, neuroprotective, or neurorestorative therapies. Neuroprotective and neurorestorative interventions are disease-modifying therapies, none of which exist today. Disease modification can be defined as treatments or interventions that affect the underlying pathophysiology of the disease and have a beneficial outcome on the course of AD. In a clinical trial the criteria for affecting the underlying cause of the disease can be supported by demonstrating an effect on a biomarker such as medial temporal atrophy on magnetic resonance imaging (MRI) or diminished tau or phospho-tau levels in cerebrospinal fluid. A delay in onset of 5 years starting 2015 results in US\$ 447 billion saving of total expected costs of US\$ 1.078 billion in the US alone.

One of the stumbling blocks of AD treatment is the time of intervention. Learning from the failures of recent drugs in clinical development, there is scientific consensus that early presymptomatic intervention appears to be the best shot. As you would imagine, delivering a therapy to people before they are even showing signs of the illness or when the illness may be in its earliest forms poses another significant challenge in designing and implementing clinical trials and in recruiting patients.

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<sup>1</sup> Alzheimer's Disease International, World Health Organization. Dementia: A Public Health Priority. April 2012. [http://www.who.int/mental\\_health/publications/dementia\\_report\\_2012](http://www.who.int/mental_health/publications/dementia_report_2012).

This makes early and accurate diagnosis and clinical trial recruitment infrastructure imperative to our efforts at achieving success.

Today, clinical testing assessing (memory function) is still the state-of-the-art methodology; there has been a great effort to ease and standardized these clinical protocols for practicing physicians. The only definite diagnosis is post-mortem when brain material is available and the tangles can be histological examined (Braak stages). Recently important advances have been made in Neuroimaging which provides prognostic value for disease diagnosis and progression. However, Neuroimaging is very expensive and not yet easily accessible.

Biomarkers have the potential to help better identify Alzheimer's patients during the pre-symptomatic stages of the disease. They have proven to be vital in therapy development efforts, particularly when dealing with a disease as complex as Alzheimer's because they help researchers understand whether or not a potential therapy is having an impact sure of an outright cure or reversal of a disease. A commonly understood biomarker would be cholesterol levels. We know that high cholesterol is a driver of heart disease. Therefore, we know that medications, like statins that lower cholesterol levels, can be effective in reducing one's risk for heart disease. Another example would be the viral load or the level of HIV in a person's blood. Medications today exist to lower a person's viral load and, in so doing, control the virus. While biomarkers are quite helpful, qualifying or validating a biomarker so that it is widely accepted by the research community and by regulators – such as at the EMA and the FDA who will be reviewing a drug to determine if it is safe and effective – is a challenge in the Alzheimer's space, a challenge that must be tackled.

Really important advances have been made in neuroimaging and biomarker research. However, their validation for disease diagnosis and progress as well as their utility of assessment of drug responses is still ongoing.

On 31 October, the European Medicines Agency (EMA) released a concept paper on the need to revise the guideline on medicines for the treatment of Alzheimer's disease and other dementias for public consultation.

New research diagnostic criteria are being used in clinical trials for different stages of the disease. In addition, a number of biomarkers to help identify and select patients at the pre-dementia stage of the disease have been developed by medicines developers; several have received a qualification opinion from the Agency's Committee for Medicinal Products for Human Use (CHMP) for use in the development of medicines.

The concept paper describes how these new developments have had an impact on recent and future clinical-trial protocols and discusses the elements to consider as part of the revision of the current guideline. These include the:

- Impact of new diagnostic criteria for Alzheimer's disease, including early and even asymptomatic disease stages on clinical-trial design;
- Choice of parameters to measure trial outcomes and the need for distinct assessment tools for the different disease stages in Alzheimer's (different signs and symptoms, differences in change over time, severity);
- Assessment of efficacy and safety in different age groups;
- Potential use of biomarkers and their temporal relationship with the different phases of Alzheimer's disease at different stages of medicine development (mechanism of action, use as diagnostic test, enrichment of study populations, stratification of subgroups, safety and efficacy markers, etc.);
- Design of long-term efficacy and safety studies;  
Usefulness of combination therapy and corresponding study designs.

## **THE G8 DEMENTIA SUMMIT AND BEYOND:**

In Europe AD has been put on the priority agenda of many governments. The health ministers from the G8 nations will meet the first ever global summit on dementia to help improve management of the disease and accelerate the development of new treatments under the leadership of the UK government.

Prime Minister David Cameron and Health Secretary Jeremy Hunt said they will use the UK's presidency of the G8 this year to spearhead "coordinated global action" against one of the greatest current healthcare challenges. I applaud Prime Minister Cameron for this leadership and urge other G8 nations to support this work at the highest level possible.

The high-level summit, which is to be held in London on December 11, will host discussion to shape an effective international solution to dementia, including looking for effective therapies and responses to slow dementia's impact.

The G8 have a unique chance to help people manage dementia better, lead healthier lives and deliver real improvements in care and substantial economic savings.

Currently, someone is diagnosed with dementia every four seconds around the globe and the disease costs more than \$650 billion a year. While 70% of this cost is incurred in 'medically advanced' nations like Western Europe and North America, nearly 60% of people with the condition live in developing countries.

The four pillars of the G8 Dementia Summit are the followings:

- 1. Building cooperation networks among governments, regulators, the private sector and the nonprofits.**
- 2. Coordination in business leading to prevention of dementia.**
- 3. Investment in solutions and treatments.**
- 4. Laying the foundations for a transition to an aging society without dementia.**

I am particularly enthusiastic and optimistic about the potential for greater levels of public-private partnership not limited to one nation or region but rather spanning the world. Such efforts are necessary if we are to achieve our shared goals of defeating Alzheimer's disease. Alzheimer's and dementia affect the entire globe and do not recognize national borders. It is a global crisis that merits a global response.

Beyond the CEO Initiative and the G8 Summit, let me provide you with a brief update on some other encouraging developments happening primarily here in Europe.

### *European Commission*

European Innovation Partnership on Active and Healthy Ageing (EIP) is a new stakeholder-driven approach to innovation, whose overarching target is to add two years to the average number of healthy life years in the European Union by the year 2020.

The Partnership is in its implementation phase: more than 3,000 partners are involved in mobilizing efforts and resources to carry forward the EIP 6 action plans:

- Prescription and adherence to treatment
- Personalized health management: Falls prevention
- Prevention of functional decline and frailty
- Integrated care for chronic diseases, including remote monitoring at regional level
- Interoperable independent living solutions
- Age friendly buildings, cities and environments

*Private Public Partnership for AD Clinical Trials (EPOC-AD)*

Greater cooperation and collaboration between academia, government and industry could enhance the drug development process. A public-private partnership is proposed to promote more efficient clinical trial designs and execution of clinical trials aimed at preventing AD dementia. The plan would create a precompetitive space to enable collaboration for optimizing patient selection, clinical trials methodologies, and candidate therapies, as well as conducting adaptive clinical trials that will produce the greatest likelihood of success.

The mission of EPOC-AD is therefore to advance this novel collaborative partnership and drive a more successful approach to drug development for preventing AD dementia. The goal is to enable rapid cycling of learning from registries and longitudinal cohorts into adaptive clinical trials that shorten timelines, improve efficiencies and permit more rapid dissemination of knowledge. A consortium of industrial, governmental and academic partners will be formed to advance this research program

EPOC-AD will conduct a continuous, global, multicenter and multi-agent clinical trial designed to efficiently identify treatments, or combinations of treatments, with sufficient promise for the prevention of halting of progression of AD to warrant definitive confirmatory testing. Basically, the trial will serve as an efficient and rigorous screen or gateway prior to confirmatory standalone trials.

**CONCLUSION:**

In conclusion, it is my earnest desire to convey to the Committee that we need the inspiring leadership of the United States government to play a key role and be a role model in facing one of the most severe and complex challenges of the 21<sup>st</sup> century. The US could play a cohesive role in helping to join hands through the G8 Summit, extending the message across to the OECD. The CEOi can be the key catalyst of all of these efforts.

Thank you again for this hearing. Although many differences exist within the international community, we share an important goal: finding a cure for Alzheimer's disease and eliminating the personal, financial and social burdens of this terrible disease. I remain confident that with united forces and the lead of your nation in a Global Action Plan, we can achieve this goal.