



Statement to the

**Senate Subcommittee on Retirement and Aging Hearing:  
The State of Alzheimer's Research: 100 Years Later**

March 20, 2007

Robert Egge  
Director, Alzheimer's Disease Project  
The Center for Health Transformation

Chairwoman Mikulski, Senator Burr, and members of the Senate Subcommittee on Aging and Retirement, thank you for this opportunity to testify regarding the significant challenge that Alzheimer's disease (AD) poses to our nation, and to the importance of responding to this growing crisis with a bold strategy that emphasizes the role of research and innovation.

My name is Robert Egge. I am a project director at the Center for Health Transformation, where I lead the Center's Alzheimer's Disease Project. The Center is a collaboration of more than 90 organizations from all segments of the health sector, including some of America's largest healthcare providers and employers.

**The Mounting Impact of Alzheimer's Disease**

As documented in the Alzheimer's Association's *Alzheimer's Disease Facts and Figures 2007* report released today, Alzheimer's strikes 1-in-8 Americans over age 65 and almost half of Americans over 85. The likelihood of developing Alzheimer's essentially doubles every five years beyond age 65. Every 72 seconds another American develops Alzheimer's disease – 50 more Americans during the course of this hearing.<sup>1</sup>

There are no cures for Alzheimer's and no remissions. It is a condition that, once begun, always leads inexorably to death – on average within eight years. These

---

<sup>1</sup> Alzheimer's Association, (2007). *Alzheimer's Disease Facts and Figures*.

are long, exhausting, and painful years, described as “the funeral that never ends.”<sup>2</sup> One caregiver recounted her experience since the onset of her husband’s condition:

*Twelve years later, my own vision has forever been clouded by seeing my husband’s brilliant mind unravel, his eloquence turn to gibberish, my name and our life together lost in the tangles and plaques that clog his brain. His identity has been stolen forever by this cruelest of disease, yet his body lingers intact because it never got the message from the brain that it is time to shut down. So together we are trapped in the endless wasteland of Alzheimer’s disease that offers no mercy to its victim or the caregiver or the family.*<sup>3</sup>

The impact of Alzheimer’s, on a national scale, is just as alarming. The Alzheimer’s Association now estimates that more than 5 million Americans suffer from this brain-crippling disease. With the aging of the Baby Boomers, this number is set to nearly triple in little more than a generation.<sup>4</sup>

Because Alzheimer’s steals independence and complicates the treatment of co-morbidities, it is already America’s third most expensive disease.<sup>5</sup> Claims for Medicare beneficiaries with Alzheimer’s disease, for instance, are three times larger than the claims of those without.<sup>6</sup> Estimates of the disease’s current cost to the nation range as high as \$200 billion per year. This year the Federal government will likely spend more than \$120 billion of this amount through the Centers for Medicare and Medicaid Services (CMS).<sup>7</sup>

Looking ahead, however, this \$120 billion tab is only a fraction of what awaits our nation. Without medical breakthroughs, as the Boomers pass through their elder years federal spending on Alzheimer’s care will increase to more than \$1 trillion per year by 2050 in today’s dollars.<sup>8</sup> That’s more than 10% of America’s current gross domestic product. With this amount of money on the table, the government simply will not be able to solve its looming fiscal problems if it fails to address this growing epidemic.

---

<sup>2</sup> Ballenger, J., (2006). *Self, Senility, and Alzheimer's Disease in Modern America: a History*. Baltimore: The Johns Hopkins University Press, as cited in, Comer, Meryl, “Be Heard Here First: A Strategic Voice for Alzheimer’s Advocacy,” *Alzheimer’s & Dementia* 3 (2007) 58-61.

<sup>3</sup> Comer (2007) 59.

<sup>4</sup> Hebert, LE; Scherr, PA; Bienias, JL; Bennett, DA; Evans, DA, (2003) “Alzheimer Disease in the U.S. population; Prevalence Estimates Using the 2000 Census.” *Archives of Neurology*. 60 (8): 1119 –1122.

<sup>5</sup> Koppel, R, (2002). “Alzheimer’s Disease: The Costs to US Businesses in 2002.” *An Alzheimer’s Association commissioned report*.

<sup>6</sup> Lewin Group, (2004).. “Saving Lives, Saving Money: Dividends for Americans Investing in Alzheimer’s Research.” *An Alzheimer’s Association commissioned report*.

<sup>7</sup> Lewin Group, (2004).

<sup>8</sup> Lewin Group, (2004).

Yet as daunting – and, in personal terms, tragic – as this portrait is, we also have sound reason for optimism about what can be accomplished if our nation commits to supporting the development of more effective therapies, guided by a bold but balanced Alzheimer’s strategy. This optimism is important, because while complacency is a grave danger, so is resignation.

## **A Record of US Biomedical Progress: Past and Present**

Our nation’s mounting Alzheimer’s crisis is largely a result of our past biomedical accomplishments. Alzheimer’s grows more common with age, and we have been remarkably successful at extending the average American’s lifespan. The life expectancy of Americans expanded by three decades over the course of the 20<sup>th</sup> century alone, increasing from 47 to 77 years of age.<sup>9</sup>

Steady progress has continued in recent decades even as the biomedical community has shifted its attention to the more complicated constellation of diseases associated with aging. In fact, according to the most recent statistics available from the CDC, the age-adjusted death rate for nine of the top ten causes of death in America fell from the prior year, including for cardiovascular disease and cancer.<sup>10</sup>

As it happens, the only one of these top-ten causes of death to increase was Alzheimer’s disease. And it will continue to increase, in step with our aging population, unless and until an effective, disease-modifying therapy becomes available.

The good news is that Alzheimer’s disease is now receiving steadily increasing attention from our biomedical research community. One accepted way to gauge the growth of scientific activity within a field is through the volume of studies on the subject published in research journals. Less than 100 articles were published on Alzheimer’s disease during the 1960s. During the 1990s, almost 25,000 such articles were published. This represents a seven-fold increase, decade on decade, over the latter half of the 20<sup>th</sup> century.<sup>11</sup>

This rapid increase in research activity continues. Nearly 52,000 scientific articles related to AD have been indexed in the PubMed database since the first such publication in 1949. Remarkably, about half of these articles have been published since the start of the new millennium, vividly illustrating the stunning acceleration of AD research.

---

<sup>9</sup> National Center for Health Statistics, (<http://209.217.72.34/aging/TableViewer/tableView.aspx?ReportId=357>).

<sup>10</sup> Miniño, Arialdi M., M.P.H.; Melonie P. Heron, Ph.D.; and Betty L. Smith, B.S. Ed., (2006). “Deaths: Preliminary Data for 2004,” *National Vital Statistics Reports*, Vol 54, No 19.

<sup>11</sup> Ballon, Daniel, Ph.D., (2007). Correspondence.

Alzheimer's research is not just rapidly expanding in its own right. It is also beginning to close a once large gap with other biomedical research fields. The comparison with cancer research is typical. From 1950 to 1980, oncology researchers published approximately 1000 papers for every one on Alzheimer's disease. By the 1990s, however, that gap had closed to a much closer ratio of 25-to-1, and so far this decade the ratio is just under 20-to-1.

This upswing in Alzheimer's disease research activity tracks closely with the commitment to significantly expand support for Alzheimer's research through the National Institutes of Health. In particular, the rapid "catching up" in the 1980s corresponds with President's Reagan's initiation of a serious, directed effort to fund AD research through the NIH. This linkage suggests that Federal government support for basic research can indeed trigger a dramatic expansion of research activity and of new knowledge.

For all the increased effort, however, AD research has not been easy work, and it's not likely to become so anytime soon. Like many other neurodegenerative conditions, Alzheimer's disease is extremely complex. Our neuroscience community has learned much about the brain, the central role it plays in regulating almost all aspects of health, and the profound disruptions to its activity associated with plaques and tangles. But those discoveries only skim the surface of the mysteries that remain.

Nevertheless, our neuroscientists are meeting this challenge, systematically unlocking the brain's complexities with ever greater strides in scientific capabilities and sophistication. Never before in human history have so many scientists worked so productively, routinely employed such sophisticated instrumentation, collaborated worldwide so effectively, and developed their discoveries so efficiently.

One result of the rapid expansion of research described above has been a series of specific, cumulative breakthroughs in our understanding of Alzheimer's mechanisms, and in the creation of novel strategies to disrupt them – with almost all these advances occurring within just the past twenty years. At the moment there are more than 250 active Alzheimer's disease trials underway as listed on [clinicaltrials.gov](http://clinicaltrials.gov). These trials are all designed to test critical aspects of our understanding of AD, helping us to put together the pieces of the puzzle that explain this disease.

These trials, as well as the underlying research strategies, have been supported by rapid advances in instrumentation and platform technologies. Some of these essential tools and methods include:

- *Imaging.* Advances in brain imaging technology – in particular, functional magnetic resonance imaging (fMRI) and positron emission tomography (PET) – are providing important clinical diagnostic aids for AD research.

Particularly encouraging is the development of novel PET scan probes/tracers that permit real-time visualization. Similar tracers are under development for use with fMRI.<sup>12,13</sup>

- *Biomarkers.* Extensive efforts are underway to identify AD-specific biomarkers that reliably and non-invasively track AD onset and progression so that, among other uses, these markers can indirectly measure drug response and help optimize treatment regimens. Researchers are currently working to identify superior markers using technologies from genomics, proteomics, metabolomics, computational and systems biology, and mathematical modeling.
- *Screening Methodologies.* A candidate therapy's performance is routinely measured using a variety of techniques including cell-based (*in vitro*) assays and animal models (*in vivo* assays). While the animal models are the gold standard, they are time consuming and extremely costly. Recently, the development of automated, high-throughput assays has greatly enhanced *in vitro* approaches to screening. Scientists are currently developing new computer-assisted (*in silico*) or virtual techniques to analyze and model the physiochemical properties of a compound in order to predict how it would behave in a complex system like the human body.
- *Animal Models.* Better understanding of the mechanisms underlying AD, coupled with advances in the fields of genetics, bioinformatics, and molecular biology, has led to substantially improved AD animal models. A major limitation of the early mouse models of AD was that the mice only developed some of the hallmark pathologies of the disease. Researchers recently addressed this problem by creating a triple transgenic mouse model that progressively developed both plaques and tangles, and demonstrated cognitive defects.<sup>14</sup> This particular transgenic mouse promises to be a valuable animal model for evaluating potential AD therapeutics.
- *Genome-Wide Association Studies.* Rapidly evolving technologies – such as computerized databases containing reference human genome sequences and tools that can rapidly identify genetic variations – are equipping neuroscientists to employ new investigative methods such as genome-wide association studies (GWAS).<sup>15</sup> For instance, one such study

---

<sup>12</sup> It is important to note that the development of these tracers, however, is comparable in process, time scale, and financial investment to the development of AD therapies themselves.

<sup>13</sup> Not only are these advances in imaging technology extremely important for research, but continued increases in capabilities with declining costs may eventually enable wide-scale, routine screening to detect AD upon onset when therapies are likely to be more effective.

<sup>14</sup> Oddo S et al. Triple-Transgenic Model of Alzheimer's Disease with Plaques and Tangles: Intracellular Ab and Synaptic Dysfunction. *Neuron*, 2003;39:409-421.

<sup>15</sup> <http://www.genome.gov/20019523>.

reported earlier this year uncovered that faults in the SORL1 gene are associated with an increased risk of late-onset AD, providing promising new avenues for follow-on research.<sup>16</sup>

The range of these research breakthroughs and others like them indicates the complexity of the task we have set before the neuroscientists in our research institutes and industry laboratories. It's as if we've asked them to build a house, but to do so they also have had to invent and fabricate all the tools needed for construction along the way. They are proving more than equal to this challenge.

Even with rapid advances in our understanding of the disease and in the tools available to neuroscience researchers though, the development of therapies – bringing them from the point of discovery to the moment of delivery – remains a high-risk enterprise. AD drugs have low clinical success rates, similar to those of other central nervous system (CNS) drugs (~8%).<sup>17</sup> Approximately 60% of drugs targeting the CNS successfully complete phase I clinical trials. Of these, ~ 40% successfully complete phase II clinical trials, and ~ 50% of these successfully complete phase III clinical trials. Finally, only ~ 70% of those that progress past phase III trials will become registered.

The new instrumentation and methodological options described above should improve these attrition levels. However, AD therapy development will remain daunting for the foreseeable future. It will continue to require substantial investments to be made by biopharma and medical device companies far in advance of what are, at best, uncertain prospects at the close of their development cycles.

### **Still Needed: A Roadmap to Guide our Alzheimer's Disease Efforts**

So today, as we look at the national projections for Alzheimer's disease, we find cause for grave concern. As we survey the progress being made in our nation's laboratories, we find reason for cautious optimism. What we will not find anywhere, however, is an excuse for complacency.

America must work both quickly and effectively to meet the challenge Alzheimer's poses to the country. And to do so, our efforts must be guided by a comprehensive, coherent strategy. What's alarming is that based even on a cursory review of our current federal efforts, the evidence suggests such a strategy is lacking.

---

<sup>16</sup> "The neuronal sortilin-related receptor SORL1 is genetically associated with Alzheimer disease." *Nature Genetics* 39, 168 - 177 (01 Feb 2007).

<sup>17</sup> Kola I and Landis J. Can the pharmaceutical industry reduce attrition rates? *Nature Reviews Drug Discovery*, 2004;3:711-715.

We have two fundamental objectives with respect to Alzheimer's. One objective, as described above, is to find therapies that will derail this disease. The second objective is to support those coping with Alzheimer's devastating impact. The first is to deliver a decisive medical solution. The second is to help reduce the pain and exhaustion, however inadequately, until medical advances make AD caregiving no longer necessary.

Both are essential goals and one might reasonably assume that the federal government is putting roughly comparable resources behind each of them. In fact, however, the imbalance in investment is startling. For every dollar the government spends through Medicare and Medicaid to help Americans cope with Alzheimer's impact, it invests less than a penny to find a cure through the work of the National Institutes of Health and the Food & Drug Administration.

This penny-on-the-dollar approach might be called America's Katrina strategy for Alzheimer's disease. As we now know, policymakers long neglected funding the work required to repair and strengthen the levees that might have saved New Orleans from the worst of Katrina's impact. And so, after the hurricane, a hundred-fold more had to be spent to rebuild the devastated city after the levees failed.

So long as the government's current, reactive posture continues, we are repeating the tragic misjudgment of Katrina every 72 seconds as another American braces against their personal hurricane with no levees to shield them.

Far from sensationalizing the present situation, in one very significant regard this Katrina analogy understates the deficiency of our current federal approach toward AD. For, however slowly, the fact remains that New Orleans is now being rebuilt. That city is recovering from the mistake of neglecting its levees. But until effective therapies are in hand, we simply have no way to even begin to restore the lives of those now gripped by Alzheimer's.

However, we do know how to go about this the right way. Our national response to HIV/AIDS shows what can be accomplished when our federal government mobilizes around a coherent, aggressive, innovation-oriented strategy. In the mid-1980s, projections for the future impact of the AIDS epidemic, absent effective treatments, were of a scale similar to what we now face from Alzheimer's disease.

In a recent interview in *Health Affairs*, NIH Director Elias Zerhouni recalled his experience as a doctor at Johns Hopkins during the mid-1980s, a time when there was not yet an effective treatment available for the disease.<sup>18</sup> Half of all beds were being used to care for terminally ill AIDS patients, and Dr. Zerhouni and his colleagues projected that within a decade, 80% of their beds would be used to care for those dying from HIV/AIDS.

---

<sup>18</sup> *Health Affairs*, 25, no. 3 (2006): w94-w103.

However, through a combination of strong research funding and accelerated FDA review, a preemption strategy yielded dramatic results. In just five years between 1995 and 2000, deaths fell 70% and survival rates increased by ten years. Results continue to improve this decade. While much more remains to be done, within the US an HIV/AIDS diagnosis is increasingly regarded as a chronic disease rather than a death sentence.

The fiscal impact of these new therapies has been equally dramatic. In his testimony before both the Senate and the House last year, Dr. Zerhouni explained how this innovation-focused strategy has saved \$1.4 trillion in healthcare expenditures,<sup>19</sup> on the basis of \$10 billion invested in basic research between 1985 and 1995; a return on investment of 140 to one.

It is time for America to once again act in a similarly bold, strategic manner, revitalizing our commitment to defeating Alzheimer's disease. If we do so, I am hopeful that in 20 years' time a future NIH Director will use Alzheimer's disease to illustrate how smart, aggressive action changed the course of the nation and immeasurably improved the lives of millions of Americans.

Thank you.

---

<sup>19</sup> <http://olpa.od.nih.gov/hearings/109/session2/testimonies/nihbudget.asp>.



## Appendix 1

### The Center for Health Transformation

#### *Preparing the Country for the Alzheimer's Epidemic: A View from Science, Business, Government, and Caregivers*

November 14, 2006

**Newt Gingrich**  
**Founder, The Center for Health Transformation**

#### **Excerpted Remarks**

[Complete remarks available at [www.healthtransformation.net](http://www.healthtransformation.net)]

This particular conference was inspired in part by an article in the Washington Post called "Open the Door to Curing Alzheimer's: Why this Research Must Become an Urgent Priority," by Bob Essner at Wyeth. It really led me to ask the question, "Are we at a turning point where the scientific knowledge base makes it plausible that you could design a roadmap of extraordinary power that could in fact provide dramatically better futures for people?"

The breakthroughs for this disease are real and they're extraordinarily exciting, and they are driven by fundamental breakthroughs in science. I want to suggest to you that we are at the edge of an opportunity that is truly extraordinary, but that requires a willingness to think beyond the normal.

If you were to look at what the cost would have been to have fixed the levees prior to Katrina and what the cost has been since then, you would see a perfect case study of prevention and failure. And one of the great challenges for the Congress and the President to confront is that if we allow annual budgeting to define our investment strategies, we guarantee in the baby-boomer retirement years catastrophic disasters, because you never generate the resources to make the breakthroughs to avoid the catastrophes, and this has been very evident in the last five or six years. I mean, it is a process; it literally fits the model of penny wise and pound foolish from the 18<sup>th</sup> century phrase that you should never try to save a penny if it cost you a pound in British terms. In our case, it is million-dollar wise and trillion-dollar foolish. And it's just utterly irrational. And yet it requires you to say, okay, what would an investment strategy approach look like?

Let me also say that one of the things that is most stunning – if you take the five-year cost of a breakthrough – if you could get a research advance that would delay the onset of Alzheimer's by five years, which is not complete victory,

but a non-trivial breakthrough, the difference would be a 40 percent reduction and prevalence – 5.3 million lives saved, a \$444 billion annual Medicare saving, a \$70 billion annual Medicaid savings, and a total \$515 billion savings for the Center for Medicaid and Medicare services. You can multiply that number by about seven to get the private savings for human beings who are using their own money today to deal with the challenge of Alzheimer's in their family. That's what just a five-year delay means as a difference.

I believe that the scale of change we need – and I'm just going to go over this very briefly but I want to set a stage here – the scale of change we need starts with how do you maximize the evolution of imaging capabilities so that you can have a very inexpensive real-time capability on a routine basis. Ultimately, in the long-run, you want brain scans to be comparable to getting your teeth X-rays, and that's largely a research – it's a combination of the National Science Foundation, NIH, Siemens, General Electric, and other systems that focus on it. But that's a box that has to be dealt with.

The second box is to design both basic and applied research tracks to essentially try to figure out what are the six or eight or nine biggest breakthroughs we need? And what level of resourcing does that require, and what level of access to data does that require? We're entering a world where if you look at Kaiser Permanente, the Veterans Administration, a number of other fairly large systems, we have over 30 million electronic health records today. We have a potential capacity to build Framingham-style studies to give you the epidemiology of a wide range of things, and we don't use them very well because we don't think like that. And so you want to look at could you identify every person who is in an early onset Alzheimer's situation out of the 30 million we already have electronic health records for and how could you knit them together into a learning system?

But this whole notion, we have to fundamentally reassess what do we mean by basic and applied research in the information age. And how do we maximize the rate of change and maximize the rate of discovery? And how do we bring together – it's very parallel to what Andy began doing at the National Cancer Institute in trying to accelerate the evolution with cancer. We need the same kind of pattern and we need to recognize, because of the emergent nature of brain science, which is at a much earlier stage than oncology, that you really want a lot more National Science Foundation involvement, because a fair amount of this is physics and mathematics; and you want NIH involvement and you want the corporations. And you want some kind of public/private research partnership to build a very high-tempo process.

The third thing you want to do, frankly, if I can take a few seconds to preach in public here, is we need an FDA brain science model of operation. Brain sciences are different. They're going to cut across all sorts of existing FDA systems. They require a level of sensitivity and intuitiveness, because today, it is

my understanding as a non-scientist, we actually determine for sure you have Alzheimer's during the autopsy. Well, that defies all the FDA requirements for figuring out who the subjects are. And so we really need to fundamentally from the ground up erase the blackboard and say, okay, in this newly emergent science involving one of the two or three largest items facing the American people, what is it we need to understand to maximize the rate of testing and maximize the rate – and again, I want total federal testing from a human safety standpoint, but I want it done in a brand new kind of framework.

This is particularly important because – my sense, again, as a non-scientist but as a historian who looks at the evolution of technology – my sense is you're going to see three parallel patterns going on simultaneously. You're going to see symptom management where you get a breakthrough that is partially palliative. It makes a huge difference if you can manage the symptom. You're going to get actual disease management. How can you in fact suppress the effect of it, make it better? And third, you are eventually going to start getting disease prevention or literally disease suppression. Now, those three tracks need to simultaneously be coordinated because you want to make progress on all three, and you don't want to give up any one of those waiting for some kind of magic breakthrough.

Fourth, I think the Center for Medicare and Medicaid Services and public policy in general, including the Veterans Administration and the federal employee health benefit plan and Tricare should all be looking from the [caregiver] side back. What is the optimum way to help people be good caregivers? What is the optimum public policy to maximize the opportunity for families to have decent lives while struggling with this terrible disease? What is it we can do, for example, we should have a center which is developing the maximum number of tools that would help people who are caregivers.

Alzheimer's Disease is a newly emergent problem that is no different than the epidemics of the 19<sup>th</sup> century or the famines of the 18<sup>th</sup> century or the industrial-era diseases of the 20<sup>th</sup> century. It's something we're going to have to learn to solve. We have to be practical about it. And the more aggressive we are and the more innovative we are, the faster we'll be successful.

And so I'm thrilled to have a chance on behalf of the Center for Health Transformation to thank all of you for being involved and to say that we very much want to work with you.

## Appendix 2

### The Center for Health Transformation

#### *Preparing the Country for the Alzheimer's Epidemic: A View from Science, Business, Government, and Caregivers*

November 14, 2006

**Samuel Gandy, M.D., PH.D., Director  
Farber Institute for Neurosciences**

#### **Excerpted Remarks**

[Complete remarks available at [www.healthtransformation.net](http://www.healthtransformation.net)]

This is the first time in medical history we can actually contemplate rational therapy for Alzheimer's disease. One of the numbers that you might or might not have heard before, but just to reinforce – half of the over-85 population has a dementing illness. That is, if both parents live to 85, statistically the likelihood is that they will – one of them will have Alzheimer's disease; will have a dementia, usually Alzheimer's disease.

So here's my title, "A Pivotal Moment is Within Reach" and that's absolutely certain; there's no doubt about that. We are now entering human clinical trials that will tell us if what we are fairly certain is true about Alzheimer's disease is in fact provable in humans.

Alzheimer's is really characterized by three key criteria. The first is the characteristic change in memory, typically the inability to form and retrieve new short-term memories. Equally frequent, patients with Alzheimer's may present with changes in personality. Eventually, all of the outside surface of the brain, all of the cerebral cortex, the part that's responsible for thinking, all of that part of the brain degenerates and patients die bed bound in what we call a vegetative state.

There is very early on a profound loss of a chemical called acetylcholine. This is a chemical that nerve cells use to talk to each other called a neurotransmitter. The currently approved medicines, at least three of the four, all target this deficiency; that is, they help the brain to compensate at the very earliest stages of the disease. However, for these medicines to be effective, intact nerve cells are required. So once nerve cells become impaired to the point of degenerating, those medicines that we currently have wear off. So these medicines don't appreciably slow the progression of the disease and don't really attack the underlying pathology. And that's what I'm going to talk about -the

accumulation of the abnormal, gummy structures. This is really what's been the heart of the advances in Alzheimer's science.

This is what has the scientific community so excited about Alzheimer's disease - amyloid plaque, a clump, a build-up of a gooey material in between nerve cells. These plaques are composed of a protein called the beta amyloid peptide. So the real problem in Alzheimer's disease, in particular, and in other aggregation diseases, is that normal proteins, proteins that are always with you all throughout life, somehow, for reasons that are often mysterious – not always – change their shape, and in this altered shape, they then plump. And that's really the bottom line.

Within the past few years, we've now been able to develop – we the field; we, not me – have been able to develop PET scans that allow the visualization of amyloid buildup in the brain during life. So for the first time in a living human, you can watch amyloid buildup.

This is an incredibly important breakthrough and is being evaluated worldwide now, especially for the testing of new medications because now, for the first time, we can see the target; we can see what we are aiming our drugs at because we're developing these anti-amyloid drugs, and most peripheral markers have not been satisfactory. This particular imaging tool is being added to a large international initiative called the Alzheimer's Disease Neuroimaging Initiative and these particular scans are supported by a project from the Alzheimer's Association.

You will hear that there's a controversy over amyloid. Is this a cause or an effect? And the likely answer is both, because we know there is some instances in which the disease begins with amyloid and we know that there are other forms in which we can't trace the exact beginning. But all the evidence indicates we are better off without this misfolded form..

Even if amyloid is not the whole story in common Alzheimer's, we know very well that these clumps in nerves, and if we look at nerve cells in a dish, are poisonous. So this is not good. The only way now we can really resolve how much of the dysfunction in Alzheimer's disease is due to amyloid is in human clinical trials in which we develop successfully anti-amyloid agents, purge the brains of humans so there's no amyloid left, and see what happens cognitively. Ideally, we'd like to actually be in the prevention mode so that we identify ways to screen people, begin anti-amyloid interventions, and prevent the scenario from ever happening. But we won't know how bad amyloid really is until we purge it completely and follow the clinical outcome.

All the strategies that are currently being tested really fall into one of three categories. The first is the immunotherapeutic approach, the vaccine. The second is a new group of compounds called plaque busters (anti-aggregation

drugs) And the third category are drug-like structures that could totally block amyloid formation.

This is really the state of Alzheimer's research. Mouse models of Alzheimer's amyloid can be caused with these amyloid-parent protein genes and cured with either vaccines, anti-aggregates, or these scissors modifiers. The real question that we're now answering in clinical trials, because these medicines are already being given to humans, is will (what we've seen in the mouse model) arrest or prevent the dementia with humans with Alzheimer's?

So I think that gives you a bit of an overview of the dramatic progress we've been able to make in the last 20 years in Alzheimer's. And the pivotal moment now is having these anti-amyloid medicines in human trials, washing the humans with these plaque-low PET scans to see if the anti-amyloid medicines work and following them with cognitive exams to see if they will stabilize or ideally, improve. And this is exactly where we are at this moment.

## Appendix 3

### The Center for Health Transformation

#### *Preparing the Country for the Alzheimer's Epidemic: A View from Science, Business, Government, and Caregivers*

November 14, 2006

**Robert Essner**  
CEO and Chairman, Wyeth

#### **Excerpted Remarks**

[Complete remarks available at [www.healthtransformation.net](http://www.healthtransformation.net)]

It's really a pleasure for me to be here today and share some thoughts on the intersection between science and patient care – in other words, how Wyeth and the private sector research-based pharmaceutical industry are trying to harness science to overcome Alzheimer's disease

I'm pretty certain that still the population at large does not really see Alzheimer's disease as an epidemic, at least not yet. Last year, I spoke at the White House Conference on Aging, and pointed out that if you were to say the word epidemic then – and maybe still today – I bet most people would immediately think about avian flu, the so-called bird flu that's on the front pages of newspapers still all the time. And it's received massive attention in the media and people are genuinely and understandably frightened about the possibility of this new disease sweeping the world. But with all the intense interest around avian influenza, I sometimes think we've lost sight of the fact that this disease or potential disease, scary as it is, is only a potential threat, and that we may or may not actually have to deal with it.

The next disease probably most people would think about as an epidemic is HIV/AIDS. Reports in the 1980s of the devastation of AIDS quickly garnered widespread attention. The fear factor of this new disease with dramatic mortality rates was extraordinary. Scientific advances and a significant amount of effort across a multiplicity of stakeholders have rendered the threat of AIDS today to be very different than the way it was 10 or 20 years ago. While AIDS does continue to ravage many developing countries, in many parts of the world today, a diagnosis is no longer an automatic death sentence. Although much remains to be done in that field, in many ways, this is kind of a miraculous fact. And I think it feeds the imagination of a world in which AIDS is no longer an epidemic, but a

manageable chronic illness. Unfortunately, obviously the same cannot be said about Alzheimer's disease.

Many people do not know that Alzheimer's disease is the third-most costly disease to treat in the United States right now, and most do not know that annual medical care costs for beneficiaries with Alzheimer's are expected to increase 75 percent over the next five years, and that federal and state Medicaid spending for nursing home care alone for Alzheimer's patients is expected to nearly double by the year 2025.

The costs of Alzheimer's disease don't strike governments alone; they also strike individual families and businesses like ours. Over the course of the disease, Alzheimer's patients and their families spend more than \$200,000 on healthcare for a patient, and employer's use approximately \$60 billion a year on lost productivity as adult caregivers are forced to leave their jobs, either permanently or on a temporary basis to care for a family member with the disease. I think you get the picture.

What is so horrifying about Alzheimer's is not just that it kills, but that it is debilitating and dehumanizing. Alzheimer's essentially eats away at the very essence of its victims, not just their physical and mental capabilities, but also, as you saw, their personalities and the qualities that I think we all believe make us human. Yet the general public still does not, by and large, consider Alzheimer's disease to be an epidemic, but the world's scientists are not just sitting by and watching the devastation approach. Efforts to respond to the epidemic of Alzheimer's are underway across academia, industry, and government.

We at Wyeth are trying to do our part. Wyeth has been researching innovative treatments for Alzheimer's for more than 15 years now. We have more than two-dozen projects in our pipeline, and have over 350 people in our research group who work exclusively on Alzheimer's disease today. And we have projects ranging from very early development through later-stage clinical trials. Our projects today use all of our available technology platforms, drugs, biotech skills, and vaccines because we want to explore every option available to us.

Wyeth is not alone obviously on this path to trying to find a solution to Alzheimer's. There are other companies at work, as well as scientists and academia and research institutes, who are making their strong contributions. The scientific, pharmaceutical, and research communities have been seeking to identify and develop new therapeutic targets that could dramatically alter the treatment for Alzheimer's. There are a lot of people on this path, and a few dozen programs each have the potential to fundamentally transform the treatment of this disease.



So why, given all the attention across various stakeholders, does the war against Alzheimer's disease continue to progress so slowly? I consider the greatest challenge facing Alzheimer's is the lack of a coherent strategy to respond to this disease. Unlike my examples of AIDS and avian flu, there is no global or even national focus on Alzheimer's. Scientific work and drug development go on, but at too slow a pace. Public health agencies are perhaps understandably engaged in dealing with the current devastation of the disease as much as working towards its cure, and regulatory agencies sometimes deal with Alzheimer's in the cautious way they do with diseases where major therapeutic options already exist. On the regulatory front alone, worldwide cooperation between reviewers and researchers could significantly improve the probability that we will succeed and reduce development times by years.

The reality is that our efforts against Alzheimer's are moving at a pace that is in no way commensurate with the problem that we're all trying to solve. What we need is a sense of urgency analogous to what arose around AIDS

What we also need is a sense of urgency driving a coordinated response to this disease. Scientists and academia, government and industry must work and in hand with regulators, healthcare providers, and patients and caregivers. We need the kind of bold innovative effort that has been generated in the past, and the AIDS story I think is instructive and inspirational. If we approach Alzheimer's with the same fervor, we'll be able to harness the potential of scientific advances and truly alter the course of this epidemic.

## Appendix 4

### The Center for Health Transformation

#### *Preparing the Country for the Alzheimer's Epidemic: A View from Science, Business, Government, and Caregivers*

November 14, 2006

**Andrew C. Von Eschenbach, M.D.  
Commissioner of the U.S. Food and Drug Administration**

#### **Excerpted Remarks**

[Complete remarks available at [www.healthtransformation.net](http://www.healthtransformation.net)]

Listening to the Video and Dr. Gandy's scientific presentation took me back to my roots. My roots at M.D. Anderson, where I spent 26 years living with this dual reality, which on one hand allowed me to be a part of what have been some of the most profound breakthroughs in biomedical research in science and in technology, and yet at the same time every single day being confronted with the suffering and death and the ravages due to a disease like cancer.

And I knew that those two realities needed to be and could be reconciled; that all of that progress, the kind of progress that Dr. Gandy talked about this morning, could now lead us to a point where we no longer had to witness and tolerate that suffering and death, whether it was a disease like cancer or the ravages of Alzheimer's. That is within our grasp. That is our opportunity. That is why this meeting and your involvement and participation are so important.

Almost five years ago, I had the privilege to come to Washington to lead the National Cancer Institute with that vision, with that passion and with that commitment, and set a goal that we would focus and commit our effort to eliminate the suffering and death due to cancer, and bring that about by the year 2015.

I would present that same perspective to you this morning, that as you are engaged passionately and appropriately in seeking and driving for a solution to the problem of Alzheimer's, you also are involved and a part of a larger transformation, a transformation in health, in healthcare, and in fact in our healthcare delivery system.

We are together collectively cooperatively in the midst of being able to change the entire future of health and healthcare. By embracing and fully

developing across the continuum of discovery, development, and delivery the new molecular reality and the molecular opportunity. And it holds the promise for being able to radically conquer diseases like Alzheimer's. Not only is the magnitude of change that significant, but the pace of change is equally significant, such that we no longer need to think of time horizons that are something in decades and centuries away as we did in the past, but to see this as not evolution but revolution in medicine.

As we look at this new future of discovery and development and delivery, I now have the privilege to have moved from the National Cancer Institute, where we had the opportunity to drive the agenda of our understanding of molecular mechanisms of a disease process like cancer, and begin to think about that disease not as an event but as a process in which those genetic and molecular and cellular events occurred over a period of time, and offered us ample targets for intervention that could preempt its outcome, the suffering and death.

And one's listens to this morning's presentations and recognizes that that is exactly the same paradigm for Alzheimer's. It is a disease process that occurs over time, and as we understand the fundamental mechanisms, as outlined by Dr. Gandy, we can begin to develop interventions, as presented by Bob Essner, that could be prevent or preempt, or modulate that disease process in a way that we eliminate the outcome, that tragic, horrible outcome that we witnessed on that video.

The FDA is positioned as the bridge that needs to be responsible for making certain that all of the fruits of that discovery and that development come to be applied to patients who are in need. And it is the FDA's commitment to be that bridge, to be that bridge not of the past, but to be that bridge of the future. And for that, like you, and like every other part of this equation, FDA must change. It has a proud record over the past hundred years of being the world's gold standard, but the FDA of the past is not adequate or equipped for this new reality, and therefore it must change, and it must change not in isolation, but in context and in collaboration and integration with all of the other parts and pieces of the equation.

And so we have embarked upon an opportunity to look internally about what those transformations are that must occur within the agency itself, and what those opportunities are to collaborate and integrate both on the discovery and development end of the continuum, as well as on the delivery end of the continuum to bring that process about.

For example, Critical path – and the need to fully implement many of the strategic initiatives in critical path so that we bring the new science that is making possible discovery and development into the regulatory process; The use of biomarkers instead of simply waiting for the kinds of outcomes that were alluded to earlier this morning having to do with autopsy findings; The ability to

completely revamp our clinical trials process and to begin to look at different adaptive trial designs and models that are adapted to the new realities; To begin to bring tools of modern information technology and bio-informatics into the regulatory process; and To collaborate and cooperate with the industry in being able to assure that we are effectively, proactively facilitating the development of these new interventions in ways that assure not just their efficacy but their safety, and to be able to stay invested not only on the front end of their development, but also to continue to monitor and modulate the behavior once they are being applied to much larger populations.

One of the things that we have done is to begin to look at ways in which we can bring the advocacy groups more actively into the process. The patient consultant program will of course include the ability to bring advocate participation into FDA's regulation and development of new treatments for serious neurological diseases, and the patient representative program will welcome your participation in advisory committees.

We have created an FDA interagency, neurology working group that will enable us to integrate across the entire portfolio of the FDA – our opportunities to begin to look at use of neurologic diseases, like Alzheimer's, as a model, just like we can look at cancer as a model through the activities that we have around the interagency oncology taskforce to drive this integrative and collaborative process.

There is much for us to change and much for us to do. This meeting typifies what we need. We need knowledge coming from scientists. We need commitment coming from the developers of these interventions. We need visions coming from public leaders, like the Center for Health Transformation, and we need leadership, and advocacy, and passion coming from you. And collectively, cooperatively, together, we will create a new world, not just for Alzheimer's or cancer, but also for everyone. You have the opportunity to help make that happen.