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Thank you to Senators Mikulski and Burr and the other members of the Subcommittee for holding this second hearing and allowing me to testify on a topic that is very important to me, my company Wyeth, and Alzheimer's patients and their families. It is my pleasure to share my thoughts on how the private sector is trying to harness science to overcome Alzheimer's disease.

I'd like to address three key points with you today:

- Alzheimer's disease is a public health epidemic facing the nation and as a result it requires an epidemic-level response.
- There is a tremendous amount of activity in the private sector aimed at identifying and developing therapeutic candidates to alter — or even prevent — the progression of this disease. My company Wyeth is a leader in these efforts.
- Our efforts would be greatly aided by a focused national strategy targeting Alzheimer's disease.

**Alzheimer's as a Public Health Epidemic**

This is an important time to be thinking about Alzheimer's and evaluating whether we are prepared for the coming epidemic. I say "epidemic" because that's what we're headed for — an epidemic of enormous proportion. I know many of the members of this Subcommittee understand the scale and scope of what we are facing. But despite the wealth of data documenting the threat of Alzheimer's

disease, I am fairly certain that the population at large does not really see Alzheimer's disease as an epidemic — at least not yet.

I have spoken about the pending threat of an Alzheimer's epidemic for several years now. During each of those opportunities — from the White House Conference on Aging to the Visions Roundtable Wyeth co-hosted with Newt Gingrich and the Center for Health Transformation — I expressed my concern that the term “epidemic” does not raise the specter of Alzheimer's disease for most Americans. Instead, most people think of diseases like Avian flu or AIDS. There has been massive media attention on these two diseases. This attention served to focus people's fear about the unknown on these diseases and highlighted their potential for decimating the population.

These fears are not entirely groundless. AIDS, particularly in the developing world, and Avian flu are serious concerns and should be matters of national interest. But it is important to remember that Avian flu — scary as it is — is only a potential threat that we may or may not actually have to deal with. And while AIDS does continue to ravage many developing countries, in many parts of the world a diagnosis is no longer an automatic death sentence.

Unfortunately, the same cannot be said about Alzheimer's disease. This is a very real threat that we do have to deal with, and at this time a diagnosis *is* a death sentence.

I have spent a great deal of time asking myself why avian flu and AIDS resonate as epidemics, but Alzheimer's does not. Is it their impact on the public health or the public's imagination? Is it the scientific etiology of the diseases or their widespread threat? Is it that AIDS and avian flu are “new” — that they were identified and discovered within our lifetimes?

Frankly, I think that the latter question is the pertinent one. Alzheimer's disease was first identified 100 years ago. It seems to have always been with us. We cannot remember a world without Alzheimer's. As a result, I think it's possible that we've simply gotten used to the presence of this disease. But that is a mistake. The disease is no less dangerous and carries no lesser burden simply because it predates all of us. If anything, the fact that the disease has continued virtually unabated for 100 years should draw our attention all the more.

Alzheimer's disease dramatically affects the public health and stirs the public imagination, and we know what its impact will be — we can, in fact, predict with chilling accuracy its incidence and prevalence. A half-million new cases will be diagnosed in America every year, as 78 million baby boomers turn 65, the typical threshold age of the disease. That could mean 14 million people suffering and dying from Alzheimer's in our lifetime.

The fact that startles me the most is that one out of every one hundred 60 year olds will develop the disease, because this year I turn 60. And if you are lucky enough to miss the disease at 60, there is the even more startling fact that one out of every two people over 85 will develop it. If my wife and I live to 85, that means that one of us is likely to be stricken by Alzheimer's.

We know the horrifying and ultimately fatal course of this illness. We know the collateral damage it does to the families of those who suffer from it — damage that often ironically carries a worse toll than the direct impact of the disease on its victims. And we can project with reasonable precision the enormous financial toll that caring for patients who suffer from it will take on our country's health care budget and our economy.

Many people do not know that Alzheimer's disease is the third most costly disease to treat in the United States. And most do not know that annual

Medicare 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 for Alzheimer's patients is expected to nearly double by 2025.

And these estimates are limited to cost of care alone. Consider the staggering cost of Alzheimer's from a more holistic perspective: A new economics study announced yesterday by the ACT-AD Coalition calculated for the first time the combined monetary equivalent of supposedly subjective social issues like quality-of-patient life, productivity and longevity. If we could mobilize treatments to delay the onset of Alzheimer's by 1 to 3 years, this social value would reach \$3.97 trillion in the U.S. alone by the middle of this century.

But the costs of Alzheimer's disease don't strike governments alone — they also strike individual families and our nation's businesses. Over the course of the disease, Alzheimer's patients and their families spend more than \$200,000 on health care per patient. And employers lose 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.

And while the economic picture is certainly grim, the social picture is even worse. What is so horrifying about Alzheimer's is not just that it kills but how it kills — it is the debilitating and dehumanizing nature of this disease that strikes me so forcefully. Alzheimer's essentially eats away at the very essence of its victims — not just their physical and mental capabilities but also their personalities and the qualities that make us all human. As the disease progresses, everything falls away — connections, understanding, relationships, and even family. The threat of Alzheimer's is here, it is very real, and it needs to be stopped.

## **The Private Sector is Responding to this Epidemic**

The general public still may not consider Alzheimer's disease to be an epidemic. But the world's scientists are starting to do so. They are not just sitting by and watching the devastation approach: Efforts to respond to the epidemic of Alzheimer's are under way across academia, industry and government.

I would like to share the story of my company, Wyeth, and our journey into the field of Alzheimer's disease research. Wyeth is not the only company engaged in the fight against Alzheimer's. Important work is occurring everyday across the industry, with nearly all of the world's major pharmaceutical companies devoting time and resources to this disease. We are proud of our position as a leader in Alzheimer's research and of our pipeline — which is second-to-none in the industry.

### ***The Genesis of Wyeth's Involvement in Alzheimer's Disease***

Wyeth has been involved in Alzheimer's disease research for 15 years. Our research efforts were focused in the year 2000, when a group of our scientists came to me with a proposal. They wanted to enter into collaboration with another, much smaller company to advance a new technology against Alzheimer's. The team members told me that this was, in their opinion, the single best approach to creating a really effective treatment for this disease and that they thought it had the highest chance of success of anything in development. I, of course, had to ask a few questions.

First, why were they so enthusiastic, and why did they think we had any chance of success in a disease that had proven so elusive? They explained that this technology was aimed at quickly ridding the brain of the beta-amyloid plaque that was — and still is — thought to be an important causal factor in Alzheimer's and that the work done so far on this principle in animal studies had produced the most dramatic results ever seen in these types of tests. So, second, I asked them how long it would take before we would have any real idea about whether

or not this would be useful in people because we all know that animal work, particularly in diseases involving the brain, is not very predictive. They told me that they expected it would take about three or so years of research effort before they would know whether the project could move into full-scale development. Then I asked them a critical question: How much would we have to spend over those years to get even a preliminary appraisal of efficacy? After a little hemming and hawing, they told me they thought it could cost up to \$100 million to do those studies.

Then I asked the really hard question: If we invested that much money over the next three years, what was the probability that when we were done with that work the answer would be "yes" — that we would have sufficient preliminary evidence about the drug's safety and efficacy to move into the larger-scale research studies necessary for approval. This brought a lot more hemming and hawing and a little shuffling about until someone said, "There's maybe a 30 percent probability of success," — to which I responded, "Really!" Then someone said, "Well, maybe it's more like 10 percent." When I challenged that, the real answer came out — which was that the odds of success were so low that no one could say what they were. In the end, we made the decision to go ahead — our scientists were so passionate that if I had turned them down, I would have had a mutiny.

Wyeth created a partnership with the Irish company, Elan Corporation. It was an unprecedented effort in that, for the first time, we brought together scientists from Wyeth's three research divisions. We asked leaders from our central nervous system drug discovery and development units to work in day-to-day collaboration with some of our leading biotechnology specialists and experts from our vaccine research effort.

The problem-solving abilities of these scientists, together with those of our partner, have brought to this project the unusually broad array of scientific tools and creativity that have kept us going. More than five years have gone by since we made our decision, and about all I can say after years of effort is that the program still has the tantalizing possibility of success. The development of our initial research program was stopped when we saw some early signs of a safety issue in a few patients. But we've come back with revised approaches, and our program is progressing very nicely.

### *Where We Are Today*

Wyeth has the most extensive pipeline of Alzheimer's discovery and development programs in the industry. We have been working on this disease for the past 15 years, and are focused on identifying and developing novel approaches to it. Wyeth has spent over \$450 million on Alzheimer's research in the past five years — \$125 million in 2006 alone. Nearly 3,000 of our scientists are or have been involved in this work, and over 350 are focused exclusively on it. Currently, we have 23 projects in various stages of development, across each of our technology platforms — pharmaceuticals, biotechnology, and vaccines. Of these, 12 are drugs in clinical research.

Wyeth is uniquely positioned to pursue novel approaches precisely because of our ability to work across these three platforms. As the only biopharma company with a presence in all three areas, we are able to draw on a wide pool of technological capabilities. Our Alzheimer's disease work is a great example of this.

I think the most exciting part of this research is the work we are doing on compounds that show the potential to delay, halt or reverse the progression of the disease — or even to prevent it altogether. These projects bring together our biotech and small molecule neuroscience capabilities. Our most advanced

projects are in passive and active immunotherapy, undertaken with our partner Elan Corporation. The passive approach uses an engineered monoclonal antibody to target toxic beta-amyloid, a substance many believe is a key cause of Alzheimer's. The active approach focuses on the use of the body's own immune system to clear the brain of the toxic amyloid plaques by stimulating an immune response so the body produces antibodies that attach to existing plaques and destroy them. These approaches represent some of the most promising efforts in Alzheimer's research today.

We are also working on a number of alternative anti-amyloid approaches, including gamma secretase and plasminogen activator inhibitor small molecule pharmaceuticals. And we are also working on treatments targeting the symptoms of Alzheimer's disease. Our symptomatic therapy efforts include serotonin antagonists and a novel oral medication that seeks to modulate neurotransmitter pathways to improve cognitive dysfunction. Our scientists believe the key to Alzheimer's treatment likely lies in combination therapies, bringing together agents to affect the course of the disease and those to manage its symptoms.

As you can tell, we intend to leave no stone unturned in this fight. We are targeting multiple approaches because we believe that it is crucial that we explore all possible avenues. While we believe the beta-amyloid theory is very likely to be a key causative factor, and therefore a promising target, we understand there may be other factors. There are still too many unanswered questions about the human brain and this disease, and we intend to pursue as many targets as possible until those questions are answered.

And, by the way, that \$100 million estimate has long ago been spent — in fact, our partnership has invested well over twice that. Our programs have the potential to be the kind of new tool we need to treat or even prevent Alzheimer's



disease — if we get really lucky. But risks are high, and, in the current environment, even if things go perfectly — which they rarely do — we still are looking at potential approval toward the end of this decade. I can tell you with complete candor that if this were a program in virtually any other disease, it would have been terminated years ago.

But the power of this disease and the challenge of conquering it drive us on. Wyeth is not alone on this path in trying to find a solution for Alzheimer's; there are other companies at work, as well as scientists in academia and research institutes who are making their own contributions.

### ***Industry-wide Efforts***

But Wyeth is not alone on this path. Important work is occurring everyday across the industry, with nearly all of the world's major pharmaceutical companies devoting time and resources to this disease. There are hundreds of therapies in development, and the first compounds with the potential to actually change the course of the disease are starting to reach FDA. The possibilities for improving the lives of patients and families are staggering.

Among the leading drugs in development for disease modification, many of the most advanced agents are, like Wyeth's leading efforts, targeted at beta-amyloid. These compounds include immunotherapy as well as agents targeting amyloid aggregation and synthesis. In addition to these late-stage therapies, there are over 100 other potential disease-modifying candidates in early-stage development with similar targets. Wyeth and other companies are targeting other mechanisms in the disease, including mechanisms that target tau, the protein that accumulates in neurofibrillary tangles, and neuroprotection.

There are also over 80 symptomatic therapies in various development stages, many of which are believed to have the potential to significantly improve the quality of life of people with Alzheimer's, particularly when used in combination

with the coming disease modifying agents. And generic versions of the leading symptomatic therapies are expected in the next several years, as the existing products reach patent expiry.

In addition to the identification and development of promising drug candidates, there are significant research efforts into better diagnostic and screening tools. Currently, establishing a clear diagnosis of Alzheimer's disease is difficult, particularly in early stages. Nearly 50% of patients are only diagnosed after the disease has already progressed to its middle stage.

One reason for this is a reluctance to assign a diagnosis of Alzheimer's disease, given the current state of treatment. But perhaps the most significant challenge is the difficulty in distinguishing signs of cognitive decline from normal aging, as we currently lack a sensitive and specific biomarker to aid diagnosis. Surrogate endpoints and biomarkers have the potential to dramatically alter how we identify patients — and potential patients — and measure their clinical outcomes over time, and their development is a major focus of the scientific efforts around Alzheimer's disease.

An example of these efforts is the Alzheimer's Disease Neuroimaging Initiative, or ADNI, a five-year public-private partnership. It brings together industry, academia and the National Institutes of Health to validate biomarkers and develop neuroimaging tools. This broad-based effort has the potential to dramatically alter how we predict the onset — and monitor the progression — of Alzheimer's. Diagnosis and monitoring are essential to any effort to study and eventually control this disease.

### **With Your Help, We Can Move Even Faster...**

So why, given all the attention across various stakeholders, does the war against Alzheimer's disease continue to progress so slowly? There are a number of significant challenges facing Alzheimer's drug development. Among them:

- Challenges related to the design and implementation of clinical trial protocols
- The lack of urgency about the disease at a national level
- The lack of scientific consensus about what it means to “modify” the course of the disease rather than merely treat its symptoms

The problem is that while companies like Wyeth are moving forward as rapidly as possible, the war against Alzheimer’s is multi-faceted, requiring advances on many fronts. Unlike my examples of AIDS and Avian flu, there is no 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 toward its cure. And regulatory agencies sometimes deal with Alzheimer’s in the cautious way they do 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.

While we are seeing a growing awareness about the Alzheimer’s epidemic, this growth is gradual and not keeping pace with the growth of the problem. It is critical that we increase the national focus on this disease and accelerate efforts to respond to it.

What we need is a sense of commitment analogous to that which arose around AIDS or Avian flu. In the war against AIDS, government, regulatory agencies, scientists in industry and academia, and patient groups worked hand in hand to develop new therapies and to evaluate them as rapidly as possible. The results were remarkable. AIDS was first identified around 1980, and, just six years later, there was a breakthrough medication that helped people manage the symptoms. And, today, there are a number of therapies that, when used in combination,

allow people with HIV/AIDS to live much longer than anyone would have dreamed possible in the early 1980s. The war has not been won, but we have made significant progress — progress that is lacking on the Alzheimer's front.

To that end I would like commend Senator Mikulski for her legislative efforts in this area. I would like to particularly note the provision in S. 898 that calls for Secretary Leavitt to convene an Alzheimer's summit. Alzheimer's disease needs to move to the forefront of our national research agenda, and this proposal is a very good start.

Knowing all of this, how do we convince the nation that Alzheimer's is the next epidemic and truly drive a change in the way the disease is approached? Public awareness of the disease is high — so are assumptions, misconceptions and complacency. To many, the disease is still seen as a slow, progressive and inevitable step in the aging process; in fact, the disease can progress through its entire course in as few as three years. This misperception, compounded by the lack of treatments with long-term effectiveness and the social stigma attached to the disease, results in a health care system that often appears to be focused more on dealing with the seemingly inevitable devastation of the disease than in working toward its cure.

Existing therapies for Alzheimer's disease address symptoms of the disease, but not its underlying causes. With the aging of the population, there is a critical need for therapies that will modify — or even halt — disease progression. We believe that this urgent need for innovative therapeutic agents warrants a formal governmental strategy to accelerate development of safe and efficacious disease modifying treatments.

The government has been successful in this area before. We need the kind of bold, innovative effort that has been generated in the past. The AIDS story is

instructive and inspirational. The recognition of the urgent need for innovative therapies led to the development of new procedural strategies for drug review and approval and to the focusing of research efforts — and dollars. If we approach Alzheimer's with the same fervor and the same commitment, we will be able to harness the potential of scientific advances and truly alter the course of this epidemic.

Within the pharmaceutical industry as a whole, there are dozens of Alzheimer's compounds in development. And, given the complexity of Alzheimer's, no single organization has the resources required to research all facets of this disease as quickly as we must. At Wyeth alone, we've committed hundreds of millions of dollars toward this research and we know our colleagues at other companies are doing the same. Right now, no one can say that any one approach will work. But, by taking multiple "shots on goal" in our research labs, we believe that a treatment can be found.

But it is imperative for industry, scientists and government to work together to help us reach our goal even faster. It typically takes 10 to 17 years to bring a new drug to market, but this is far too slow, given the imminent threat. We need a sense of urgency, a commitment to collaboration that will lead to a concerted, focused effort to prevent this impending epidemic. To eradicate Alzheimer's, we need to make it America's number-one research priority. We need the public and private sectors — the pharmaceutical industry, health-care practitioners, the public, and legislators — to call for putting epidemic-strength resources toward eradicating Alzheimer's.

For every month we hesitate, millions more Americans will tangle helplessly in the disease's lethal net and we will continue to find ourselves spending down the nation's health care budget to care for the demise of millions of people. More wisely, we should be preparing now to cure them. We could make my

generation the last to dread Alzheimer's. It is time to accelerate the pace of our efforts and take the battle to a level on a par with our hope.

As I mentioned earlier, I turn 60 this year. I have been a witness to the impact of this disease and have watched family and friends fall prey to it. Without tools like those that Wyeth is currently developing, the impact on our budget — and our psyche — will devastate our nation. The suffering that individuals and families endure must not be extended to our entire country. If we cannot develop therapies to halt this epidemic, we will either face untenable systemic costs that break our national bank or we will be put into the equally untenable position of having to deny treatment to those who need it.

I commend you for your efforts and look forward to working with you in the war against Alzheimer's. If we can generate a passionate commitment analogous to that around AIDS or avian flu, I believe that within our lifetime we can turn this disease from a death sentence to a treatable chronic diagnosis. The sooner we begin, the better.

Thank you.