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Chairman Kohl, Ranking Member Corker and honorable members of the Committee, thank you for inviting me to testify here today. I respectfully request that my full written statement be submitted for the record.

My name is Tony Adamis and I am the Vice President and Global Head of Ophthalmology at Genentech. I am an ophthalmologist and vascular biologist by training. Prior to joining Genentech in 2009, I served in other positions in the biopharmaceutical industry, as well as eleven years on the full time faculty of the Harvard Medical School. At Harvard, I led a laboratory studying the mechanisms of eye diseases, including age-related macular degeneration and diabetic retinopathy.

My role here as part of the committee's look at drug pricing, particularly in medicines used by older Americans, is to discuss Lucentis (ranibizumab injection), the Genentech medicine approved for the treatment of a number of eye diseases worldwide. This discussion comes in light of recent studies that compare the use of FDA-approved Lucentis with the off-label use of Genentech's cancer drug Avastin (bevacizumab injection) in an eye disease called wet Age-Related Macular Degeneration (wet AMD). The results of these studies demonstrate that Lucentis improves vision with fewer ocular injections than Avastin[1], and that Avastin may be associated with an increased risk of serious systemic side effects[1-3]. For these and other reasons I shall review today, Genentech believes that physicians should be able to prescribe the medicine that they and their patients determine is most appropriate.

As we all know, pricing is not a simple issue. To help the committee members better understand the many factors that contribute to the price of Lucentis, I will review the story behind the creation of Lucentis and how it differs from Avastin, the costs associated with the development of Lucentis, and the enormous impact the medication has had on patients suffering from eye disease. All of this I hope will create an understanding that pricing is part of a larger development model that results in breakthrough treatments for patients.

GENENTECH MISSION

Genentech was founded around the discovery of recombinant DNA technology and was the first company to develop medicines from living cells. In so doing, Genentech launched the biotechnology industry 35 years ago. In 2009, Genentech became a member of the global Roche group. Genentech is headquartered in South San Francisco, and as part of the Roche group currently employs over 30,000 people in the United States. By employing Americans in high-skill, high-wage jobs, Genentech/Roche impacts not only patients, but also the recovering US economy.

Genentech's commitment to future innovation is unparalleled within the industry, with more than 100 projects in clinical development. In 2009, Genentech/Roche spent $9.1 billion on research and development, an amount greater than any other company in the world, including Microsoft, Toyota and Apple.[4] Genentech's R&D investments are directed towards developing innovative medicines to treat serious diseases. One of the most impactful medicines we have ever developed is Lucentis.

CLINICAL IMPACT

<u>Age Related Macular Degeneration (AMD)</u>

Before Lucentis was developed, "wet" age-related macular degeneration (wet AMD), was the leading cause of blindness in Americans over the age of 50.[5] Wet AMD occurs when abnormal blood vessels grow beneath the light-sensing tissue of the eye, the retina. When these vessels hemorrhage and leak, vision is degraded. As

recently as 2005, the average wet AMD patient progressively lost central vision over several years, until the ability to read, recognize faces and drive was diminished or lost. In addition to the personal suffering and loss of independence, the total annual cost to the U.S. gross domestic product due to lost wages was estimated to be $5.4 billion.[6]

That situation changed with the development of Lucentis. Genentech's Phase III trials demonstrated that the average patient treated with Lucentis *recovered* vision – a result never before seen in wet AMD. Vision improved after the first dose and reached peak levels approximately 4-6 months later. When these results were first announced in the summer of 2005, the President of American Society of Retinal Specialists publicly compared Lucentis to the discovery of penicillin. FDA approval was obtained in 2006, and the impact in the United States since then has been sizable. A recent publication estimates that the rate of legal blindness in wet AMD patients treated with Lucentis has been reduced by 72 percent.[7] As a result, wet AMD is likely no longer the leading cause of blindness in Americans over the age of 50.

Retinal Vein Occlusion (RVO)

Genentech also developed Lucentis for a second major cause of vision loss and blindness, retinal vein occlusion. The disease typically has a sudden onset and in the worst cases can lead to total blindness. Genentech's Phase III clinical trials demonstrated that Lucentis dramatically reduced the rate of vision loss and produced sizable visual gains. FDA approval was obtained in 2010.

Diabetic Macular Edema (DME)

Diabetic retinopathy is the leading cause of legal blindness in working age Americans, representing a large unmet medical need with significant economic consequences. The most common complication of diabetic retinopathy is diabetic macular edema, or DME. Since 1985, DME, has been treated with laser therapy, a procedure that clinical trials showed slowed the rate of vision loss.[8] Our recent

Phase III data show that Lucentis produces significant vision gains in these patients. The beneficial effects were evident after the first treatment and have lasted two years. Three-year data will be available next spring. Approximately 75,000 new cases of DME are diagnosed each year in the United States.

Surveys have shown that people over the age of forty have a significant fear of going blind, and that blindness is feared more than premature death.[9] Lucentis has prevented blindness and restored vision in countless patients. I believe it is not an overstatement to say that it has changed the course of many lives.

THE COST OF DEVELOPING LUCENTIS

Drug development is lengthy, expensive and risky. Data show that drugs entering clinical development have a 92 percent failure rate.[10] Lucentis was one of the 8 percent that succeeded. The price of Lucentis funds not only its own development, but also the 92 percent failure rate and future successes.

Lucentis has gone through rigorous Phase III development programs that have clearly established a favorable risk/benefit profile. To date, 11 years and over $1.1 billion have been spent on completed clinical trials with Lucentis, involving more than 7100 patients around the world. This sum does not include ongoing development trials, investigator sponsored trials, the 11 years of research prior to human testing, our extensive safety monitoring, or the establishment of expensive manufacturing and analytical sites around the world that produce Lucentis and assure its quality. In short, the Lucentis development program has been one of the most expensive in Genentech's history.

LUCENTIS HISTORY

The Lucentis story begins in 1989, when a Genentech scientist discovered vascular endothelial growth factor, or VEGF. Dr. Napoleone Ferrara characterized the DNA

coding for a novel, naturally occurring protein and demonstrated that it made blood vessels grow.[11] By the mid-1990's, his research showed that blocking VEGF may prove useful in the treatment of cancer, where blood vessel growth is required for tumor growth. Around the same time, and working in close collaboration with Dr. Ferrara, my colleagues and I at the Harvard Medical School conducted a series of experiments identifying VEGF as an important target for eye disease.[12]

While Dr. Ferrara was in the early stages of developing a VEGF antibody for cancer, the medicine that eventually became Avastin, a separate research program was started to design an anti-VEGF drug specifically for the eye. The latter medicine became Lucentis. There were attributes of the Avastin molecule that suggested it wouldn't be ideal for use in the eye, so Dr. Ferrara's team set out to create something better. In 2010, Dr. Ferrara was awarded the prestigious Lasker-DeBakey Prize in recognition for his work on Lucentis. Seventy-six Lasker laureates have gone on to win the Nobel Prize.

There are four scientific reasons why Lucentis was created. They involve drug potency, tissue penetration, ocular safety, and systemic safety. Today, because of the time limitations, I will focus on systemic safety.

LUCENTIS SAFETY

When drugs are administered to the eye, they often find their way into a patient's blood stream. When this happens, side effects are more likely. When administered to the eye, Avastin and Lucentis both enter the blood stream. Avastin was designed to treat cancer, therefore a long residence time in the blood stream was desired, so that it could have sustained activity against tumors in the body. The opposite, however, was desired for Lucentis. It was designed to exit the blood stream very quickly (hours instead of weeks) in order to reduce the risk of systemic side effects.

In the past decade, studies have shown that anti-VEGF drugs in the blood stream can result in rare, but serious, side effects. Genentech continuously monitors the safety of its drugs and takes action when potential risks are identified. When an interim

safety analysis in 2007 revealed a potential risk of stroke with the use of Lucentis in wet AMD, Genentech promptly sent a letter to health care providers, notified the FDA, updated the package insert, and presented the data to the scientific community.

Today, there is a growing body of data that suggests off-label Avastin may pose greater risks than Lucentis when used to treat wet AMD. Two large Medicare claims studies, one from Duke University[2], and a second from Johns Hopkins[3], both identified a potentially greater risk of stroke and death when using Avastin vs. Lucentis in wet AMD. Of note, Genentech funded the latter study through an unrestricted grant. Separate studies have shown that when administered to the eye, Avastin can block VEGF in the blood stream for up to 28 days.[13]

The NIH-supported CAT Trial also showed a safety signal.[1] This was the first large randomized, controlled trial to examine the safety and efficacy of Avastin in wet AMD. These types of trials are considered the highest level of evidence in medicine. The CAT Trail reported a statistically significant 29 percent increased risk of serious systemic side effects with Avastin vs. Lucentis, with over 80 percent of the side effects requiring hospitalization. Genentech's internal analysis of the CAT Trial data revealed that part of the increased risk with Avastin was consistent with VEGF inhibition in the bloodstream.

These data are not yet conclusive. However to date, it is notable that the three largest studies comparing the safety of Avastin to Lucentis have shown statistically significant safety risks with the use of Avastin in wet AMD. The combined evidence suggests that the use of Avastin in the eye may be associated with an increased risk of serious systemic side effects.

PHYSICIAN CHOICE AND ACCESS TO TREATMENT

As the data emerge on the safety and efficacy of Avastin and Lucentis in wet AMD, Genentech believes that physicians should be free to prescribe the medicine that they determine is most appropriate for an individual patient. We agree with the

American Academy of Ophthalmology that a treatment plan must be selected by the ophthalmologist and the patient, considering important risk/benefit information that empowers them to make evidenced-based decisions.

Genentech is committed to ensuring that no patient goes without treatment due to financial barriers. Since 1985, when its first product was approved, Genentech has donated approximately $2.3 billion in free medicine to uninsured patients. Since 2005, Genentech has donated more than $550 million to various independent, non-profit organizations for co-pay assistance. In 2010 alone, Genentech Access Solutions helped more than 107,000 patients with coverage and reimbursement issues.

Genentech offers comprehensive patient access programs for Lucentis. They include LUCENTIS Access Solutions® and the Genentech Access To Care Foundation. These programs provide assistance with reimbursement and coverage issues, and offer a variety of other services, including free medicine, to eligible patients.

CONCLUSION

I hope this testimony is helpful in your consideration of these important issues. Genentech is committed to working with the Congress, public health agencies, CMS and the FDA to ensure the safety and effectiveness of our products and fair payment systems that recognize innovation, and provide patients with access to needed medicines.

Today, innovation continues at Genentech, as we seek to improve Lucentis and to develop additional breakthrough medicines for blinding diseases. This work depends, in part, on the success of Lucentis.

U.S. companies are being called upon to innovate. Genentech was in fact founded with a mission of innovation, and has succeeded in treating some of most serious sight-threatening illnesses affecting Americans.

Thank you for the opportunity to provide my views today, and I look forward to addressing your questions.

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