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STATEMENT OF ROBERT J. BEALL, Ph.D.

PRESIDENT AND CEO

CYSTIC FIBROSIS FOUNDATION

BEFORE THE

U.S. HOUSE OF REPRESENTATIVES

ENERGY AND COMMERCE COMMITTEE

HEALTH SUBCOMMITTEE

REPRESENTATIVE MICHAEL BILIRAKIS, CHAIR

REGARDING

NATIONAL INSTITUTES OF HEALTH: RE-ENGINEERING CLINICAL

RESEARCH

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**Summary of Statement of Robert J. Beall, Ph.D.,
President and CEO, Cystic Fibrosis Foundation**

The Cystic Fibrosis Foundation applauds Congress for doubling the budget for the National Institutes of Health (NIH) and Dr. Elias Zerhouni for ensuring that reform of the clinical research enterprise is a key element in the NIH Roadmap. Today, I would like to share a few lessons we have learned that may be instructive to NIH as it re-engineers the clinical research program.

- A therapeutics development program must be comprehensive and include the following elements: 1) a basic research effort; 2) drug discovery; 3) clinical trials of new products; and 4) tests of existing products to determine possible new uses of them.
- A strong investment in the infrastructure of a clinical trials network will yield tremendous benefits by accelerating the testing of promising therapies.
- Strong partnerships between NIH and private nonprofit groups will be key for improving care for orphan diseases, because private industry has limited incentive to focus on rare diseases.
- In its reform efforts, NIH should heighten its emphasis on clinical research training, strengthen its collaboration with all private entities, and improve the peer review of clinical research proposals.

The CF Foundation is taking calculated risks to identify and develop new treatments for this life-threatening genetic disease, while at the same time protecting patient safety, and NIH must do the same. By re-engineering the clinical research process, the NIH assures its place as the world's biomedical research leader.

Good morning, Mr. Chairman and Members of the Committee. I am Robert J. Beall, Ph.D., President and CEO of the Cystic Fibrosis Foundation, a private nonprofit foundation with a mission of finding a cure for cystic fibrosis (CF). It is a great pleasure to appear before the Committee today to discuss the research approaches that the CF Foundation has adopted, and it is certainly an honor to appear at this hearing with Elias Zerhouni, M.D., who is providing strong and creative leadership at a critical juncture in the history of the National Institutes of Health (NIH).

In the last decade, Congress has generously increased funding for NIH. Between fiscal years 1999 and 2003, Congress accomplished the impressive goal of doubling the NIH budget. The substantial funding of NIH contributed to significant advances in basic research, including the mapping of the human genome, and deepened our understanding of a number of diseases.

It is now vital to assess our ability to translate the basic research advances of the last decade into treatment advances. The CF Foundation has, in the last decade, reformulated its own research approach to encompass many types of research, from basic research through Phase III clinical trials, and has created the infrastructure required to accelerate the development of new CF therapies. As a result, we now have a pipeline of nearly two dozen potential therapies that are being examined to treat people with CF. We applaud Dr. Zerhouni for undertaking a meticulous review of NIH, its structure, and its methods of funding research, as we believe progressive changes are necessary to ensure that NIH continues to be the biomedical research leader of the 21st century.

Living with Cystic Fibrosis

Before I present the CF Foundation's comprehensive approach to research, I would like to describe CF and its effects on the individuals living with the disease. Each year, 1,000 children in the United States are born with CF, and there are about 30,000 Americans living with CF. In 1989, CF Foundation-supported researchers discovered the gene that is altered in CF, and since that time our fundamental understanding of the disease has improved significantly.

The defective CF gene causes the body to produce abnormally thick, sticky mucus that clogs the lungs and leads to life-threatening lung infections. The thick mucus in those with CF also can obstruct the pancreas, preventing digestive enzymes from reaching the intestines to break down and aid in the absorption of food.

The common symptoms of CF include chronic cough, wheezing or shortness of breath, excessive appetite but poor weight gain, and greasy, bulky stools. CF symptoms vary from patient to patient, due to the fact that there are more than 1,000 mutations of the CF gene.

CF has been transformed to a chronic disease, but living with CF as a chronic disease requires a rigorous daily regimen of therapy. Treatments for individuals with CF include enzymes that aid digestion, antibiotics administered during bacterial infections and as a preventive measure, and daily therapy to loosen the mucus in the lungs. Several new drugs have been approved in the last decade that have improved the health of people with CF, including Pulmozyme, which thins the mucus so that it can be coughed up, enabling the individual to breathe easier and reducing the chance for infections. Strict adherence to CF treatments improves the health status and quality of life for individuals with CF, but the stringent regimen can be a physical, emotional and financial challenge for patients and their families.

When the CF Foundation was founded in 1955, people with CF often did not live to attend elementary school. Over the past five decades, the median age of survival has improved significantly and is now in the early 30s. This improvement in the life expectancy for those with CF can be attributed to research advances, which I will discuss in some detail later, and to the teams of CF caregivers who offer specialized care of the highest quality. The CF Foundation supports a nationwide network that includes 117 CF care centers at large academic and medical institutions, and a number of smaller affiliate care centers, as well as nearly 85 programs that are focused on the care of adult patients who are 18 years and older. The CF care center network ensures that information about advances in care can be immediately disseminated to all CF caregivers who provide cutting edge care to the more than 90 percent of the individuals with CF who receive care at these centers. The care center network also functions as a training ground for those who seek careers in CF care or research. Together, Dr. Zerhouni has referred to this as the CF “community of research,” as the CF community works to bring research to the bedside to improve care.

The Research Mission of the CF Foundation

The cornerstone of the CF Foundation’s effort has been to quickly put into place the critical elements necessary to translate basic research knowledge to new therapies. I’d like to share a few points with you today about lessons learned by the CF Foundation which may be appropriate for the NIH as it moves forward in the Roadmap effort.

We believe that the key to finding the cure for CF, and improving the quality of life of those with the disease, lies in the CF Foundation’s research program. There are several key elements to the CF research program that are making it successful:

- 1) ***An aggressive program to discover potential CF drug candidates.*** Although the discovery of the CF gene in 1989 was an important step forward, there is still much to be learned about the disease. As a result, the CF Foundation continues to invest in basic research on CF to deepen our knowledge of the disease and to understand how we may intervene in the disease course. During the past five years, we have committed more than \$100 million for cutting-edge technologies to aid in the discovery of new compounds for CF. We have now identified several lead compounds that we hope will begin clinical trials in CF in the next 18 months. None of these compounds would have been discovered without the application of these cutting-edge technologies.

- 2) ***Establishing a clinical trials network.*** The CF Foundation established a network for clinical trials, called the Therapeutics Development Network (TDN), in 1998 specifically to work with industry to pursue new treatments for CF. The network is a critical enticement for industry to focus on CF, as its leaders provide expert advice on trial design and its very structure facilitates patient recruitment. The usefulness and efficiency of such a network were demonstrated through collaborations in the early 1990s with Genentech, Inc. on the development of Pulmozyme and with Pathogenesis (now Chiron) on the development of TOBI. The network links key CF clinical research centers with a centralized coordinating center at the Children's Hospital and Regional Medical Center at the University of Washington at Seattle. Expanded twice, the network now includes 18 centers across the country to further enhance recruitment, while building on the core features of centralized data management and analysis, and a coordinated system

of data safety monitoring with disease-specific expertise for protection of patients. Since the TDN was put into place, nearly thirty clinical trials – including Phase I, II, and III trials – have been completed or are underway. Anyone of these drugs in clinical trials could have a major impact on the disease or provide an ultimate cure.

- 3) ***A matching awards program for companies to develop CF therapies.*** Because CF is an orphan disease – with fewer than 200,000 persons affected – it presents companies developing new drugs a smaller possible financial return than other diseases. To encourage companies to become engaged in CF drug development, the CF Foundation established the Therapeutics Development Program, which includes awards to companies to undertake research and development of promising drug candidates. We established financial collaborations with biotechnology and pharmaceutical companies to bring them into the field of CF. These commitments, ranging up to \$25 million, help companies reduce their financial risks in order to focus on CF. Most of the drugs in our current pipeline would not be tested in CF patients were it not for these initiatives.

- 4) ***Evaluation of existing drugs to determine their utility in treatment of CF.*** While the CF Foundation pursues strategies for the development of new CF treatments, it simultaneously employs a “low-hanging fruit” approach, investigating new uses of drugs that have been approved by the Food and Drug Administration (FDA). This strategy has already proven successful, with the completion in 2002 of a Phase III trial that tested the use of the oral antibiotic azithromycin in individuals with CF who had chronic *Pseudomonas aeruginosa*

infections in their lungs. The results of the trial, coordinated by the TDN, showed that those who received azithromycin three times a week for 24 weeks experienced improved lung function, gained weight, and spent only half as many days in the hospital as those who received a placebo.

Overhauling Clinical Research at CF Foundation and NIH

Our efforts to bring new drugs to people with CF reaffirm Dr. Zerhouni's vision for the NIH. There comes a time in the history of any research organization when the accumulation of critical knowledge must be translated into treatments for people with disease. The NIH Roadmap provides the opportunity for the NIH to do this. However, unless the NIH takes an active role in translation, many of the diseases for which we now have identified the gene and possess a strong understanding of their pathophysiology will never be researched, as few organizations have the financial resources to exploit the basic research opportunities to find new therapies.

When the CF Foundation undertook the establishment of the CF clinical trials system in 1998, we asked several fundamental questions about the status of the CF research effort and our ability to translate basic research findings into new CF treatments. When we read the NIH Roadmap at the time of its release in September 2003, we found that NIH, under the leadership of Dr. Zerhouni, had asked the same basic questions about the NIH. Those questions were: 1) What are today's scientific challenges? 2) What are the roadblocks to progress? 3) What do we need to do to overcome those roadblocks? and 4) What can't be accomplished by any single Institute – but is the responsibility of NIH (or the CF Foundation) – as a whole?

The answers to those questions – as they applied to CF research – led us to the determination that we had to form the TDN to streamline CF clinical trials and accelerate the translation of basic research into new treatments. We are pleased that the team that worked on development of the NIH Roadmap reached a parallel conclusion – that the clinical research enterprise supported by NIH must be re-engineered. The Roadmap recommends the integration of clinical research networks, improvements in the training of the clinical research workforce, and the development of core services for translational research initiatives. The CF Foundation applauds Dr. Zerhouni for undertaking a thorough evaluation of NIH and assembling a team to assist in the redesign of key NIH clinical trial programs.

We believe lessons learned in the CF Foundation’s TDN will be instructive as NIH proceeds with establishing clinical trials networks and will provide special insights regarding the most efficient means of conducting clinical trials on orphan diseases. Supporting orphan disease research must be a central tenet of NIH, as few in the private sector can undertake this difficult and costly work.

The Partnership Between CF Foundation and NIH

The CF Foundation has enjoyed a productive relationship with several institutes and centers at NIH. The National Center for Research Resources (NCRR), under the leadership of Judith Vaitukaitis, M.D., appreciated the CF Foundation vision for improving its clinical trials capacity and provided important early financial support for the TDN coordinating center. The support the coordinating center has received is in keeping with the NCRR mission of providing CF clinical researchers the tools they need for the efficient completion of their studies, and we look forward to a continued strong relationship with NCRR.

A number of basic and clinical CF research projects have received support from the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) and the National Heart, Lung, and Blood Institute (NHLBI), and research on the human genome – of tremendous importance to CF – has been supported by the National Human Genome Research Institute (NHGRI). We are very pleased that NIDDK recently released a Request for Applications for Cystic Fibrosis Research and Translation Core Centers to support both basic and clinical research on CF. As envisioned by NIDDK, the Core Centers will provide shared resources to support research to develop and test new CF therapies and will foster collaboration among strong CF research centers.

While the CF Foundation is fortunate to have incredibly dedicated volunteers who are willing to raise significant dollars to support the mission of finding a cure, this undertaking cannot be successful without a strong partnership with the NIH. All of these relationships with NIH institutes and centers are critical to our efforts to advance CF research.

Recommendations for Re-engineering Clinical Research

We offer several recommendations for reform at NIH. While the CF Foundation has worked productively with NIH, we believe that certain changes would strengthen the ability of NIH to advance clinical research. Most of the issues we identify below are addressed in large part by the NIH Roadmap, and we endorse its aggressive implementation. We encourage Congress to provide Dr. Zerhouni and the NIH with the tools and resources to capitalize on the potential of the Roadmap. In order to realize the benefits of the substantial investment this country has made in basic research, we must take this enterprise to the next level to benefit

Americans living with life-threatening diseases today. Toward that end, the CF Foundation recommends:

- **Improved training of clinical researchers and acceptance of clinical research as a viable career in academic medicine.** A number of blue ribbon panels have reported in recent years the various influences on young physicians that discourage them from choosing a clinical research career. If steps are not taken soon to improve training of clinical researchers and ensure these researchers a means of succeeding in academic institutions, the nation's clinical research enterprise will be crippled.
- **Collaboration among NIH, academic institutions, private foundations, and industry in NIH-supported clinical trials networks.** The CF Foundation has learned, through direct experience, that cooperation among all players must be ensured early in the clinical trials process. The involvement of industry is critical. Moreover, the traditional roles that the players in clinical trials have assumed may not be the most appropriate ones in all circumstances. For example, the CF Foundation chose to fund biotechnology companies, as that strategy appeared to be the best way to stimulate development of a new treatment. Another potential reform is action by academic institutions to streamline their research review processes to ensure that multi-institution clinical trials can function smoothly. We must all work together to facilitate clinical trials so that we can improve the health of our country.
- **The improvement of peer review of clinical research proposals through routine establishment of special emphasis panels.** As noted in the article in JAMA (2004 Feb18;291 (7):836-43), clinical research proposals submitted to NIH fare poorly when they are reviewed by basic scientists who may not have appropriate experience or

knowledge to review such proposals. In certain disciplines, special emphasis panels have been established for review of clinical research proposals. We recommend that such panels be established on a more routine basis to encourage appropriate consideration of clinical research proposals.

- **Bureaucratic obstacles to the speedy completion of clinical trials must be eliminated.** Efforts must be made to reduce duplication in the review of trials by institutional review boards (IRBs). Although patient safety must be a primary concern in any clinical trial, the current system of review allows duplication and delay without improving patient protection.

The Future of Clinical Research

The CF Foundation is committed to pursuing whatever steps necessary to bring new treatment options to people with this disease. To date, those steps have included funding basic and clinical research; in the future they may encompass other aspects of drug development if public or private collaborations are not forthcoming. Our vision is unswerving, as we have shown that we can fill a pipeline with promising options for patients. We believe the NIH must embrace the opportunity to translate the knowledge gathered from basic research to securing the development of new therapies. Just as the CF Foundation does not have all the answers from CF basic research, we believe it is essential to move forward and to take risks to find new treatments. No lives can be saved without taking risks while at the same time assessing patient safety. And, the risks of not taking such steps are unacceptable to the CF Foundation.

On behalf of the Cystic Fibrosis Foundation, I would like to express my appreciation to the Committee for holding this hearing to discuss the future of NIH. Congress has reason to be proud of its role in supporting NIH, which is the world's leader in biomedical research. The NIH has strong leadership to move into the new century, when we will see the translation of basic research into new treatments for many diseases. We believe the experience of the CF Foundation in clinical research can serve as a model for research on other orphan diseases, and we stand ready to work with NIH and Congressional leaders as they consider changes for the future.

CURRICULUM VITAE

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Men and Women in Science
National Institutes of Health Merit Award (1980)

Societies: American Association for Advancement of Science
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House Committee on Energy and Commerce

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3. Please list any federal grants or contracts (including subgrants or subcontracts) which you have received since October 1, 1999:		
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Signature: *Ray Peabo*

Date: 3/29/2005