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Written Testimony for Hearing: "21st Century Cures: Incorporating the Patient Perspective"
Committee on Energy and Commerce, Subcommittee on Health

Summary and Recommendations

This testimony will outline exciting advancements in the development of new cystic fibrosis treatments, the challenges and risks inherent in developing treatments for this rare disease, the need for a balance between accelerating treatments and ensuring they are safe and effective, and what Congress can do to help move treatments more efficiently to patients.

The Foundation's policy recommendations include:

- Ensure that patients have a voice in drug development, review and approval,
- Support the creation of mechanisms to accurately measure what meaningful outcomes are for patients,
- Support the creation of mechanisms to generate comprehensive, quality data to help make the analysis of risks versus benefits less burdensome for patients,
- Ensure a well-resourced FDA, and
- Monitor implementation of the Food and Drug Administration Safety and Innovation Act (FDASIA)

Written Statement

On behalf of the Cystic Fibrosis Foundation and all of those in the cystic fibrosis (CF) community, we greatly appreciate this opportunity to provide testimony for "21st Century Cures: Incorporating the Patient Perspective," a hearing in the Energy and Commerce Committee's Health Subcommittee. We commend the Committee for initiating this dialogue and for promoting a climate that supports the advancement of biomedical innovation.

The story of cystic fibrosis is one of hope and optimism, a remarkable example of what is possible when patients, industry and other stakeholders collaborate to develop treatments that are changing the lives of those with the disease. This testimony will outline exciting advancements in the development of new cystic fibrosis treatments, the challenges and risks inherent in developing treatments for this rare disease, the need for a balance between accelerating treatments and ensuring they are safe and effective, and what Congress can do to help move treatments more efficiently to patients.

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Cystic Fibrosis and New Genetically-Targeted Treatments

Cystic fibrosis is a life-threatening genetic disease that affects 30,000 children and adults in the United States. It is primarily a lung disease caused by a defective gene that makes the body produce mucus that clogs the lungs and leads to serious infections.

Life expectancy for those with CF has risen remarkably during the past six decades. In the 1950s, those with CF didn't live to go to elementary school – now people with cystic fibrosis are living into their 30s, 40s and beyond.

This is due in part to groundbreaking advancements in treatments that target the disease from every angle. As genetically-targeted treatments move through the CF drug pipeline and on to patients, this disease is at the forefront of a new era in personalized medicine and is a model for what can be achieved when stakeholders collaborate on the development of treatments for a rare disease.

January marked the two year anniversary of FDA approval of Kalydeco™, the first treatment to target the root genetic cause of CF in a subset of people with the disease. In the two years since its approval, many of the nearly 2,000 patients worldwide who take the treatment are breathing easier, gaining weight, and even being removed from lung transplant lists. FDA approved this drug in near record time, almost two months ahead of the drug's review date.

In another major advancement, positive data for phase 3 clinical trials for a new targeted therapy were recently released by Vertex Pharmaceuticals, evaluating the effect of a combination treatment of Kalydeco and lumacaftor (VX-809), which could treat nearly 50% of the total CF population.

The CF community was thrilled when the clinical trial data showed that people ages 12 and older with two copies of the F508del mutation who received the treatment had significant improvements in lung function and other key measures of the disease. Those receiving the combination, in addition to experiencing improved lung function, also had improved weight gain and significant reductions in the rate of pulmonary exacerbations and associated hospitalizations and IV antibiotic use. Vertex

Pharmaceuticals plans to submit a New Drug Application to the FDA for this treatment by the end of the year.

These successes, in rapid succession, represent a real turning point in the lives of those diagnosed with CF and are opening doors that could lead to a cure for CF in our lifetime.

The Cystic Fibrosis Foundation Drug Development Model and the Challenges Ahead

Getting to where we are today was a long and complex process, resulting from the Cystic Fibrosis Foundation's strategic and coordinated approach to curing the disease. The main focus of the CF model is collaboration across sectors, as the Foundation, academia, industry, government, patients and the medical community work together to develop treatments. Included in this is the CF Foundation's work to invest in basic and translational research, support the development of a clinical trials network dedicated to CF therapeutic development, initiate and enhance a patient registry including rich data about the treatment of CF patients, and advance a "venture philanthropy" model for therapeutic development.

With the success of Kalydeco and promising potential disease modifying treatments, many complicated therapy development challenges lie ahead. Although the combination therapy described above could benefit a large portion of the CF population, there are many children, teens, and adults with no therapy available to address the underlying cause of the disease. The Foundation and its partners are committed to a development program that will bring the promise of these drugs to the entire CF community.

The development program necessary to achieve this goal will be complex. We will increasingly be targeting very small segments of the orphan CF population, and conducting trials in such small populations is difficult. Trial design, trial participant accrual, and data analysis are all difficult in these trials. The CF Foundation will be bringing multiple drug developers together for various combination

trials, a complex undertaking. In addition, we believe that there will be additional "generations" of CF disease-modulating drugs, and achieving prompt accrual to these trials will pose significant challenges.

Ensuring the Balance between Speed & Safety and Efficacy

CF patients and their families have shown their commitment to the CF Foundation's therapy development program by their generosity. They contribute generously to the Foundation through financial contributions, through volunteer action, and as participants in clinical trials.

We owe it to those patients to develop the strongest possible new therapies and to ensure that the drugs we develop are safe and effective. For CF patients living with a chronic disease, the adverse effects of any drug must be weighed carefully against the therapeutic benefit.

As policy options are considered, it is important to find a balance between accelerating drug discovery and innovation, while also ensuring that patients have safe, effective treatments. Although patients are willing to take a certain amount of risk when it comes to treatment, approving therapies based on data collected early in clinical research, prior to more rigorous study, could pose a health risk for patients. We must keep in mind that positive data based on what works in the lab, or even in phase 2 clinical trials, may not translate to tangible benefits for patients.

Furthermore, it could endanger progress towards the development of other treatments. Those who receive a drug for which there are limited data may not be willing to participate in further clinical trials for other drugs to treat their illness, or be open to trying other treatments backed by better quality data.

When finding the balance between accelerating drug discovery and innovation and ensuring safety and efficacy, there must be clear communication about the benefits of current therapies so that patients can make informed decisions about clinical trial participation of new therapies and about changes in their treatment as new therapies are developed. Patients are the ones assuming this risk, and

they need to know and help define which treatments will have a meaningful impact on their quality of life.

The decisions that must be made by the FDA and patients are difficult and complex, and drug developers, physicians, researchers, patient organization and other key actors need to be forthright in communicating concrete data so they can make the most informed decisions. In this era of personalized medicine, decisions are only going to become more complicated in the years ahead.

A good example of a tool for providing patients useful data that is used by the CF Foundation is the publishing and dissemination of CF patient registry data on quality of care at accredited CF care centers. This allows patients to have comprehensive information with which to make decisions about how best to choose care providers.

What Can Congress Do?

First, Congress should work to ensure patients have a seat at the table, because no one understands a disease better than the people who suffer and fight every day.

In particular, it is important to support the development of mechanisms to accurately measure what meaningful outcomes are for patients, both in terms of clinical outcomes and their quality of life. Developing these mechanisms is challenging, but it is critically important. Providing greater resources for regulatory science at the NIH, FDA, and other federal agencies is a key component to making this goal a reality.

Congress should also create mechanisms to generate comprehensive, quality data that will make the analysis of risks versus benefits easier for patients. It is important to think creatively throughout the development cycle, especially for those drugs approved rapidly and those that are being used long-term by patients.

For example, supporting continued study after a drug is marketed to patients generates data that are vital to monitoring the long-term impact of a treatment. Right now, the CF Foundation is funding the GOAL study, enrolling patients to carefully monitor the effects of Kalydeco on an ongoing basis, and this provides invaluable insight into the long-term impact of this relatively new drug.

Finally, as the Committee develops policies to advance and accelerate treatments to patients, a crucial component is ensuring a well-resourced FDA. While funding levels are set by the Appropriations Committee, as an authorizing Committee, Energy and Commerce is a key voice in setting funding priorities for Congress.

Sufficient funding permits the FDA to be a party to early discussions about clinical trial design, allowing enough staff time for this interaction and supporting training for personnel to develop the expertise needed to effectively and efficiently review complex treatments. Adequate resources also allow the FDA to move aggressively and rapidly when the data support a new drug's approval, providing enough staff with the sophistication needed to permit rapid review.

The Food and Drug Administration Safety and Innovation Act (FDASIA) included many provisions to encourage a patient-focused drug development and review model, but not all provisions are being implemented and others are being implemented by the agency in the narrowest way. Congress can continue to monitor the implementation of FDASIA provisions at the same time it assesses the adequacy of FDA resources for targeted medicine review.

Adequate resources also allow enough time to interact with and accept advice from external experts. The CF Foundation championed the inclusion of a provision to foster FDA staff consultation with outside experts in FDASIA. We advocated this provision of the law based on our belief that FDA review staff members were unlikely to be trained in or have a strong understanding of every rare disease and complex clinical trial design issue, and that reviewers could learn much about rare diseases and rare disease therapies by consultation with experts in the field. The expert consultation provision of FDASIA

set standards to foster such collaboration and consultation. We hope that the Committee will ensure implementation of this provision of FDASIA and that the agency will embrace the spirit of the law even as it honors the letter of the law.

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Once again, we greatly appreciate the opportunity to share our experiences and recommendations and stand ready to work with you on the challenges ahead. Thank you for your consideration.

Sincerely,

Robert J. Beall, Ph.D.
President and Chief Executive Officer