Preston W. Campbell, III, MD., President and CEO, Cystic Fibrosis Foundation

On behalf of the Cystic Fibrosis Foundation and the approximately 30,000 people with cystic fibrosis (CF) in the United States, we are pleased to submit the following testimony to the House Appropriations Committee’s Subcommittee on Agriculture, Rural Development, Food and Drug Administration, and Related Agencies for fiscal year 2017. In order to encourage efficient review of drugs for cystic fibrosis and other rare diseases, we urge the Committee to prioritize the Food and Drug Administration (FDA) and provide at least $2.85 billion in fiscal year 2017. We encourage special consideration and support for the Center for Drug Evaluation and Research (CDER), its Office of New Drugs (OND), and the Office of Orphan Products Development (OOPD).

Drug approvals by the FDA reached an 18 year high in 2014, and more than 400 rare disease drugs and biologics have been approved in the last 30 years. As the agency’s responsibilities continue to grow and we enter an unprecedented era of innovation in drug development for rare diseases, even more needs to be done.

Cystic fibrosis is a rare genetic disease that causes the body to produce thick mucus that clogs the lungs and other bodily systems, resulting in life-threatening infections and other complications. There are nearly 2,000 mutations of the CF gene that can impact those with CF, and with the advent of precision medicine, therapies are being customized to treat a patient’s specific genetic makeup. As this new concept in drug development quickly becomes a reality, it opens the door for the advancement of new targeted therapies in many important areas of medicine, including cancer and rare diseases like CF.
There are currently two therapies that have been approved to treat the underlying cause of CF in more than 30% of those with the disease. One such therapy, Kalydeco, was approved in 2012 to treat 4% of patients with CF based on their underlying CF-causing mutation. The approval was subsequently expanded to treat 8% of those with the disease soon after. Kalydeco’s initial review time was three months, one of the fastest in the FDA’s history. A second targeted therapy, Orkambi, was approved in 2015 to treat the most common CF-causing mutation. Orkambi was the first drug to receive the FDA’s breakthrough therapy designation, and it underwent a six-month expedited review.

This success is a testament to what can be achieved when stakeholders collaborate across sectors to ensure a swift review of critical drugs. Throughout the review processes for Kalydeco and Orkambi, the Cystic Fibrosis Foundation and renowned CF experts worked closely with the drugs’ sponsor Vertex Pharmaceuticals and the FDA to provide insight on specific issues related to CF, clinical research on CF treatments, and other related issues. The collaboration and efficiency in these trials can serve as a model for best practices in clinical trials for rare diseases.

Since its creation, the Breakthrough Therapy Designation at the FDA has been widely successful at accelerating the approval of new treatments that demonstrate substantial improvement over existing therapies. Cystic fibrosis treatments were the first designated as breakthrough therapies, and the process has improved efficiency and communication between the FDA and drug sponsors. Sponsor requests for the Breakthrough Therapy Designation have increased dramatically since the program’s inception in 2012. In the program’s first two years alone, CDER received more than 200 requests for breakthrough designation, and more than half of the therapies that were granted an expedited review through this program were for rare or orphan diseases. Sponsor requests for this designation are expected to increase further in the
coming years, and expanded funding and support for this program is critical to ensure that new breakthrough therapies receive an efficient yet rigorous review.

As new, more advanced personalized treatments like Kalydeco and Orkambi move through the pipeline, it is critical that the FDA has the resources necessary to further develop innovative methods for reviewing and evaluating the safety and efficacy of targeted therapies. The CF Foundation has significantly expanded its research investments with leading companies to accelerate the discovery and development of new genetically-targeted treatments. The Foundation is supporting 45 studies in 2016, including examination of several new targeted therapies. One series of studies planned for 2016 has the potential to treat the underlying cause of the disease in more than 85% of those with CF. It is crucial that the FDA have sufficient funding to provide a swift and efficient review of treatments for rare, life threatening conditions where there is an urgent need for new, targeted therapies.

A number of clinical trial design issues have been identified that may arise in review of rare and precision medicine therapies. As precision medicine continues to develop, robust funding is particularly crucial as the FDA will need to find new, innovative ways to handle unprecedented challenges in drug development and review.

For example, recruiting sufficient numbers of participants to support a classic clinical trial design for a rare disease population is often not possible, simply because there is a smaller pool of patients. This issue becomes even more significant with the advent of precision medicine as therapies become targeted to smaller populations based on unique genetic mutations within the CF population. As potential new therapies come under review, it may be necessary to test combinations of drugs in populations that include patients with several different CF mutations and develop and test single and combination therapies in n of 1 trials (those that consist of a
single patient). The FDA needs adequate funding to develop new regulatory pathways and approaches to handling variations in trial design that both maintain safety and efficacy standards while facilitating the development of treatments for patients with rare diseases.

Researchers and clinicians are also concerned about executing placebo-controlled trials for genetically-targeted treatments when successful, genetically-targeted drugs are already approved and available to patients. In addition to the ethical question of asking trial participants to suspend their use of the best available therapies, there is also a concern that such a request would dissuade participation in clinical trials for the next generation of targeted therapies.

As evaluating the safety and efficacy of targeted therapies becomes more challenging, there is also greater need for the use of biomarkers and the development of additional outcome measures. Biomarkers with the potential to reasonably predict clinical outcomes could play a tremendous role in accelerating drug development and review. However, the FDA needs adequate funding to accelerate classification of biomarkers and ensure that they are being examined throughout the clinical trials process. Similarly, Patient Reported Outcomes (PROs) are a largely untapped source of valuable data and information that can help advance understanding of efficacy throughout a clinical trial. As the FDA is looking at new and innovative ways of evaluating treatments, the agency needs the resources to consider new sources of valuable data to further inform and accelerate the review process.

Overall, as drug development advances, the FDA must be supplied with the proper resources to balance the need for an efficient and rigorous review process with the flexibility required to accommodate deviations from the standard clinical trial process.

We commend the regulatory science initiative formed by the NIH and the FDA, which aims to accelerate the development and use of new approaches to evaluate drug safety, efficacy,
and quality. With additional funding, the FDA will have greater ability to partner with key stakeholders to promote discussions and workshops of study designs to maximize the progression of safe and effective therapies through the development pipeline. Collaboration of the FDA with the NIH as well as external stakeholders offers immense promise for helping to expedite the drug development process and put safe and effective drugs in the hands of patients. However, this type of collaboration cannot move forward without adequate funding.

In addition, the CF Foundation is enthusiastic about the potential for clinical trial, clinical care, claims, and other health-related data to be utilized to improve drug discovery, development, and delivery. The Foundation has been a pioneer in the development and utilization of a robust data repository through the CF patient registry, and our therapeutics development network (TDN) has successfully encouraged clinical trial partners to share data. We ask that Congress support efforts by the FDA to explore strategies and guidelines for clinical trial data sharing. As drug development research advances, data sharing is vital to the acceleration of new discovery.

This is a time of great hope and optimism for the cystic fibrosis community as more therapies that treat the underlying cause of CF move through the pipeline. However, the FDA faces critical challenges as targeted therapies are being brought up for review, including small patient populations and the need for more flexibility in trial design. Additional funding to foster stakeholder collaboration to find solutions to these challenges and encourage clinical trial data sharing will help move much-needed treatments more efficiently to those who need them most.

Once again, we urge the Committee to make funding for the Food and Drug Administration a priority in fiscal year 2017 and provide at least $2.85 billion for the agency. The CF Foundation stands ready to work with the Committee, FDA, and Congressional leaders on the challenges ahead. Thank you for your consideration.