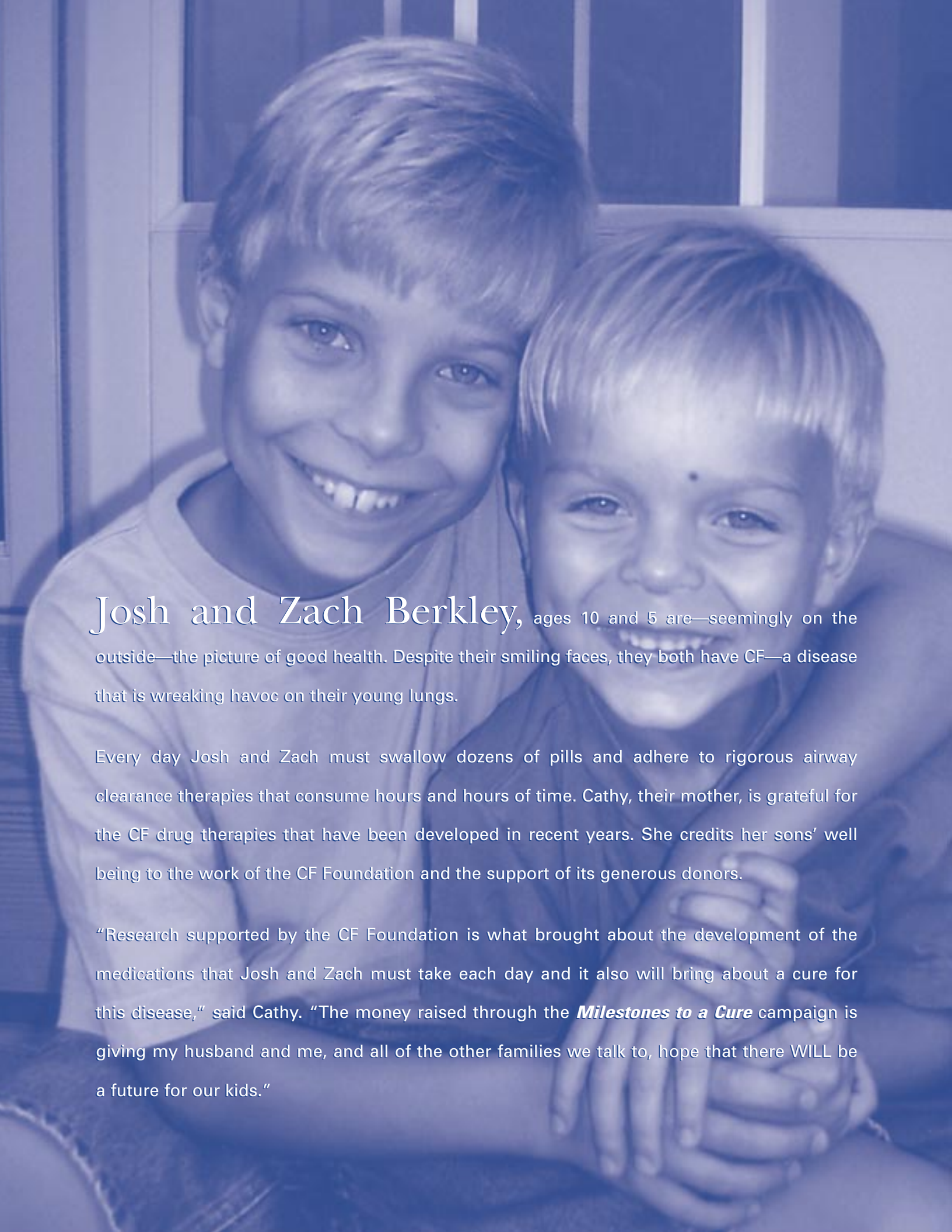


Milestones to a Cure

building a portfolio
of progress

A Case for Support

Cystic Fibrosis Foundation



Josh and Zach Berkley, ages 10 and 5 are—seemingly on the outside—the picture of good health. Despite their smiling faces, they both have CF—a disease that is wreaking havoc on their young lungs.

Every day Josh and Zach must swallow dozens of pills and adhere to rigorous airway clearance therapies that consume hours and hours of time. Cathy, their mother, is grateful for the CF drug therapies that have been developed in recent years. She credits her sons' well being to the work of the CF Foundation and the support of its generous donors.

“Research supported by the CF Foundation is what brought about the development of the medications that Josh and Zach must take each day and it also will bring about a cure for this disease,” said Cathy. “The money raised through the *Milestones to a Cure* campaign is giving my husband and me, and all of the other families we talk to, hope that there WILL be a future for our kids.”



dear friend,

My wife, Kathy, and I have experienced the devastating impact of cystic fibrosis (CF). Our son, Joey, fought the disease—bravely—for 12 years, before we lost him in 1986.

When we first learned that Joey had CF, Kathy and I knew that we would need the support of our family and friends to help us through the difficult times ahead. We also knew that it was vitally important to support the then-fledgling Cystic Fibrosis Foundation. It was developing a plan—unique and bold, yet focused—to tackle this disease in a way unlike any other charity or voluntary health organization in the United States.

For three decades, we have wholeheartedly supported the CF Foundation, often finding comfort in the fact that we could measure the amazing progress in the scientific advances in CF. The discovery of the CF gene was quite encouraging, as well as the establishment of a robust drug development program, which has already brought three CF therapies to patients. Newly diagnosed patients can expect to live into their 30s—tremendous progress relative to the three-year survival rate of Joey's "class." These milestones offer evidence and hope to all those touched by this disease that an even better, healthier future is possible. Still, far too many young lives are cut short by CF. The advances of yesterday have opened the doors of today's opportunities. In fact, for the first time ever, the opportunities to support meritorious science have outpaced the CF Foundation's ability to fund them—an unacceptable reality.

The goal of the *Milestones to a Cure* campaign is to ensure that new therapies for CF are developed as quickly as possible—and we need the support of a \$175 million major gifts campaign. The clock is our worst enemy—for every hour, every day, we lose precious lives.

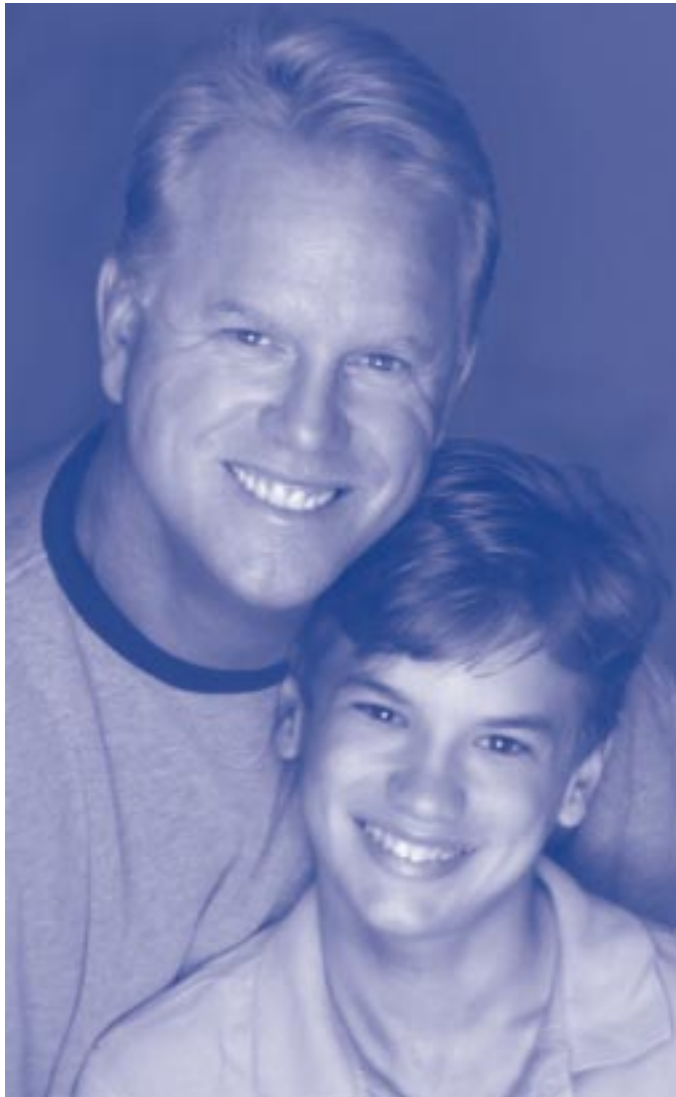
We need your help. This *Milestones to a Cure* campaign is focused on carrying our message, our track record, and our unprecedented opportunity to people like you who can change the face of this disease sooner, rather than later. We need your immediate investment in our work. The lives of our children depend upon our success. And, we will succeed.

I hope we can count on your support.

Sincerely,

A handwritten signature in blue ink that reads "Joe O'Donnell". The signature is written in a cursive, flowing style.

Joseph J. O'Donnell
Campaign Chairman



*“We know that the best possible research in the world comes through the Cystic Fibrosis Foundation. We strongly believe that this is the place to focus our time, energy and funds in order to beat this disease—that is why we wholeheartedly support the **Milestones to a Cure** campaign. We desperately need the \$175 million that this campaign will raise to support critical CF research. The future of my son, Gunnar, and thousands of others with CF, depends on it.”*

Boomer Esiason,
Honorary Campaign Chair
and son, Gunnar

building a portfolio of progress

In 1955, the Cystic Fibrosis Foundation was created by a group of parents who were determined to fight for the hopes and dreams of their children. Sadly, at that time, there were few answers to be found as CF was little known and poorly understood in the medical and scientific communities. Only a handful of specialists were treating children with the disease and their efforts were largely ineffectual. Most children born with CF in the 1950s did not live to attend grade school.

Knowing that research would ultimately provide the answers to their questions about this disease, the founding parents also knew that the fuel for driving the CF research engine forward was money. They began to reach out to family and friends to help raise the resources needed to begin an aggressive research program.

Throughout the intervening decades, the CF Foundation has achieved many milestones—markers of progress in the struggle against this debilitating disease. One of the most significant medical milestones was the identification of the CF gene in 1989. Pursuing that discovery, against considerable odds, the CF Foundation and its scientific collaborators served as pioneers in the field of genetic research. Since then, this landmark discovery has increased the understanding of the biochemical, molecular, and cellular interactions that give rise to the disease, and that cause so many with CF to struggle in their daily lives. This research also set the stage for the next phase of scientific inquiry, developing

drug therapies that can control and hopefully, one day soon, cure the disease.

To drive drug development, the CF Foundation established the Therapeutics Development Program in 1998. Through an innovative business model that seeks collaborations with the biotechnology industry, the Therapeutics Development Program has ensured that the latest technologies and the brightest minds are focused on CF. To date, this program has resulted in two dozen therapies currently being developed for CF. In recent years, three new therapies have become available to CF patients with encouraging results.

Of course, no milestone is more significant, or could ever be more relevant than those we call birthdays—the celebration of another year of life. Today, the median survival age of those with CF is 33—progress to be sure, but not a cure!

At the CF Foundation, we strongly believe that the Therapeutics Development Program will produce the results we so desperately seek. The more therapies we develop, the greater the likelihood of finding one or more that will improve the health of those with CF. Yet, the most fundamental of facts—that money buys science—will always be our greatest challenge.

With your support of the *Milestones to a Cure* campaign, we envision achieving many medical milestones and, with each of them, greater assurance for a long and full life for thousands of children and young adults with CF. Together, we can change the face of this disease, forever.



Life is often measured in milestones. For people with CF, who are often robbed of the life events others take for granted, any milestone is significant and a welcomed passage to the next stage of life.

Although people with CF are still a long way from leading "normal lives," the drug development milestones enabled by the CF Foundation make this concept a much more likely prospect.

It is the goal of the CF Foundation that all people with CF will be able to, one day, take both the drug development milestones and the milestones of life—marriage, family, career—for granted. With continued and increased support of the CF Foundation's programs, they will be able to do just that.



Facing the Challenge

Today, in the United States, there are approximately 30,000 children and adults living with CF. Although CF profoundly affects those with the disease and their families, it is known as an “orphan disease.” That is, there are too few patients with the disease for large pharmaceutical companies to justify an investment of resources in CF drug discovery and development. Drug development is an expensive and protracted business. It can take years of clinical trials and hundreds of millions of dollars to bring a new drug to market. Only a fraction (one-fifth) of all drugs entering clinical trials actually receive approval from the Food and Drug Administration (FDA). Not surprisingly, most large pharmaceutical companies hedge their bets, focusing on those diseases (e.g., heart disease or cancer) that yield the best returns. This is precisely why the *Milestones to a Cure* campaign must succeed.

Devising Our Strategy

After years of progress in basic science research, including the milestone discovery of the CF gene, the CF Foundation built a sufficient base of scientific knowledge to begin the next phase of its research program—drug discovery and development. Confronted with the realities of the marketplace, the CF Foundation devised an innovative business model to ensure a commitment to CF drug development within the emerging biotechnology industry. In 1998, the CF Foundation established the Therapeutics Development Program with the primary goal of increasing the number of drug therapies in the CF drug development pipeline. This program continues to enlist drug development collaborators in the fight against CF by offering expertise in the science of CF, access to operating capital for

research projects of potential benefit to CF patients, and an established clinical trials network (at the more than 115 accredited CF care centers) that can safely, effectively, and efficiently conduct clinical trials.

Congratulations to the Cystic Fibrosis Foundation for its innovative approaches to improving the quality of life for all people with cystic fibrosis.

William H. Gates, Sr., Chairman,
Bill & Melinda Gates Foundation

How Are We Doing?

Since the creation of Cystic Fibrosis Foundation Therapeutics, Inc. (CFFT) in 2000—the nonprofit drug discovery and development affiliate of the CF Foundation—drug development for CF has gained significant momentum. The CF Foundation provides funding to CFFT, which governs the activities of the Therapeutics Development Program. As such, CFFT’s collaborations with biotechnology firms have led to about two dozen potential CF therapies in preclinical development or clinical trials. CFFT’s largest alliance to date focuses on the basic defect of CF and has led to the identification of a number of potentially disease-modifying compounds that will, hopefully, begin clinical testing in the next few years.

Early investment by CFFT with many biotechnology firms fostered further support by other investors, leveraging the commitment to CF drug development. Three new CF therapies have been added in recent years, including Pulmozyme® (which helps clear obstructed airways), TOBI® (an inhaled antibiotic), and azithromycin (an existing antibiotic that was proven to reduce lung infections in CF patients).

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Is This Enough?

Although there is certainly considerable excitement in the CF community about the current drug development pipeline, the fact is that it is not expansive enough. History tells us that

a majority of drug compounds do not successfully make it through the rigors of the three phases of clinical testing required by the FDA.

To ensure success, we must significantly increase the number of potential CF drugs in the development pipeline. The more therapies that can be developed, the greater the likelihood of finding one or more that will improve the health of those with CF.

In addition, we must continue to seek new products that manage CF, such as antibiotics, or products that help clear the lungs. We also must intensify efforts to identify products that target the basic genetic defect. While this treatment strategy is likely to cost more in discovery, it clearly would have the greatest impact on the lives of CF patients.

Of course, the CF Foundation recognizes that while increasing the number of drugs in the development pipeline is an indicator of progress, it is the quality of those drugs that will ultimately determine if we are successful in controlling or curing this disease.

How Can We Accomplish Our Goal?

From a scientific standpoint, the CF Foundation is well positioned to accomplish its goal. The CF Foundation's willingness to embrace emerging technologies, such as high-throughput screening, and to align with firms pushing the frontiers of biotechnology, should pave the way to other CF research opportunities and milestones.

The number of potential compounds already identified as a result of high-throughput screening may very well become CF drugs in the future.

And, current efforts to understand how these compounds work also may lead to more CF drug discovery opportunities. In addition, the CF Foundation's success in adapting the antibiotic azithromycin for CF patients bodes well for seeking other pre-existing products to see if they are valuable to people with CF.

The Cystic Fibrosis Foundation has become a trend-setting organization for modern molecular medicine because of the remarkable progress made in CF research.

Francis S. Collins, M.D., Ph.D.
Director, National Human Genome Research Institute at the National Institutes of Health

A Case for Growth

Given the growing number of opportunities that are now available for CF therapeutics development, the CF Foundation projects that it will need approximately \$175 million over and above its expected spending patterns through the year 2010. Having access to a reliable stream of drug development funding will provide the CF Foundation with the ability to enter readily into agreements with biotechnology companies when promising therapies are identified, and the flexibility to focus resources on those projects with the best chances of producing effective CF drugs.

We must address these financial issues now, or our ability to impact the CF drug development pipeline will be lost. We cannot launch new initiatives without the assurance that the financial resources are there to sustain them through completion.

The *Milestones to a Cure* major gifts campaign is intended to provide the CF Foundation with the financial means to take advantage of the expanded opportunities for CF drug therapy development. If we can accelerate our growth by significantly increasing the number of potential therapies in the pipeline, we can increase exponentially our chances for successfully finding a means to control, or possibly even cure, CF.



**Our goal is to raise \$175 million,
over a period of five
years, through the
*Milestones to a
Cure* campaign...**



*“Just for a day I’d like to wake up
and not have any pain or be sick
or anything. Just once to be free.”*

Alexandra Deford
(1971 – 1980)

*“Health is a freedom, too. I never
really understood that until my little
daughter spoke these words shortly
before her brief life ended. In Alex’s
memory—in the memory of all the
dear children we have lost—may I
urge you to contribute to the **Milestones
to a Cure** campaign. So might everyone
in this world someday soon be free
of cystic fibrosis. Free... every day.”*

Frank Deford
Chairman Emeritus
Cystic Fibrosis Foundation

Milestones

- 1955** A group of parents form the Cystic Fibrosis Foundation.
- 1961** The CF Foundation establishes the first CF care centers.
- 1982** The CF Foundation establishes the first-of-its-kind network of Research Development Program centers.
- 1983** CF Foundation-supported scientists show that cells lining the lungs of CF patients fail to move chloride properly in the airways.
- 1988** The CF Foundation creates Cystic Fibrosis Services, Inc., a national mail-order pharmacy, to provide CF patients with access to CF medications. CF Services also provides patient advocacy and education.
- 1989** Scientists supported by the CF Foundation discover the gene that causes CF.
- 1990** CF researchers achieve “proof of concept” for gene therapy that “normal” genes could be added to CF cells to correct the basic defect.
- 1993** The first CF gene therapy treatment is administered to a patient with the disease and shows promise for correcting CF cells in the nasal passages.
The FDA approves Pulmozyme®—the first new drug treatment specifically developed for CF in 25 years.
- 1994** The CF Services Pharmacy is the first to dispense Pulmozyme to CF patients.
- 1997** TOBI®, an aerosolized antibiotic used to treat CF lung infections, gets FDA approval after CF Foundation-supported studies showed safety and efficacy.
The CF Foundation establishes the Therapeutics Development Program to provide matching awards to biotechnology companies to help stimulate the discovery and development of new CF therapies.
- 1998** Seven CF care centers tapped to form the Therapeutics Development Network to provide the resources and the infrastructure needed to conduct CF clinical trials.
INS37217 becomes the first drug to begin clinical trials using the Therapeutics Development Network.
- 2000** Cystic Fibrosis Foundation Therapeutics, Inc. (CFFT) established as the nonprofit drug discovery and development affiliate of the CF Foundation.
The largest CF research award commitment in the history of the CF Foundation (up to \$46 million) made to bring high-throughput screening technology to the CF drug discovery effort.
- 2001** CFFT makes multi-million dollar investment to develop a more efficient pancreatic enzyme, called TheraCLEC™ Total, that has the potential to benefit nearly all CF patients.
- 2002** Results of azithromycin clinical trial show that CF patients who took the antibiotic experienced an almost 50% reduction in hospitalizations, significant improvements in lung function and weight gain.
The Therapeutics Development Network expands to 18 CF care centers to accommodate the growing number of CF clinical trials and to provide greater geographic opportunities for CF patients to participate in clinical trials.
- 2003** A Phase II CF gene therapy trial begins and represents the largest and most advanced gene therapy trial for CF to date.
- 2004** Results from the INS37217 Phase II clinical trial demonstrate both safety and improvements in CF lung function.



Campaign Chair
Joseph J. O'Donnell

Honorary Chairs
Boomer and
Cheryl Esiason

**Campaign Executive
Committee**

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J. Taylor Crandall
Thomas J. Hughes
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Amy S. Weinberg
John S. Weinberg
Donald C. Wood

investing in the future




Robert J. Beall, Ph.D.
President and CEO
Cystic Fibrosis
Foundation

For the first time, CF research opportunities are outpacing our ability to fund them. Without additional revenue, discoveries will be missed, potential therapies will be stalled, and more young lives will be lost. That is why we have initiated the *Milestones to a Cure* campaign. This campaign, and its goal of infusing \$175 million into the Therapeutics Development Program over the next five years, represents a monumental milestone in its own right—an unequaled commitment to ensure that CF science continues to move forward at an accelerated pace.

The value of new therapies to people with CF has the tangible effect of stemming the ravages of the disease, but also an intangible effect—offering hope and optimism to individuals and to the CF community at large. However, it is sobering to note that potential therapies for CF will not be pursued without additional financial support from the CF Foundation.

People with CF need more success stories from the drug development pipeline. The framework for these successes has been set in place. The *Milestones to a Cure* campaign must be successful to keep the CF research momentum moving in a positive direction. By investing in this campaign, you will help us build our portfolio of progress and increase the speed at which a cure is found.

For decades I have witnessed the toll that CF takes on the patients and their families. Aside from the disease itself, our greatest challenges are time and a need for more funding. Your support of the *Milestones to a Cure* campaign is an investment in saving lives. We cannot allow potentially lifesaving research to come to a standstill—too many precious lives are counting on us.



Stacy Danko, R.N., B.S.N., has enjoyed more milestones in her life than she or her family ever expected. Diagnosed with CF when she was 6 months old, she was not expected to live past the age of 18.

Now in her early 40s, Danko is the mother of three healthy children, a registered nurse, and a risk management administrator for a state agency. She credits her ability to achieve these milestones, in part, to the advances that have been made in CF research and care.

“When I was young, the treatments for CF were few and knowledge of the disease was limited. Thanks to the efforts of the CF Foundation, so much more has been learned about what causes CF and how to ensure a better quality of life for people like me,” said Danko.

As Danko reflects, “There are a few more milestones that I want to attain—to watch my children grow up and to have families of their own. Your support of the ***Milestones to a Cure*** campaign is giving me the much-needed hope that I will be able to achieve those dreams.”



The mission of the CF Foundation is to assure the development of the means to cure and control CF and to improve the quality of life for those with the disease.



...adding tomorrows every day.

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