HEALTH ADVOCACY
Cystic Fibrosis

One patient's story, and the future of cystic fibrosis

Living with advanced-stage CF, this woman helped build Emily's Entourage to push research for the patients left behind. She's still waiting for what comes next.

Emily tours the labs and facilities at Translate Bio during their CF Awareness Month event.

Emily Kramer-Golinkoff is only 41 years old, but she knows intrusive machine noises and constant physical pain all too well. Living with advanced-stage cystic fibrosis (CF), her days are filled with hours of airway clearance, breathing treatments, and taking pills, and she has CF-related diabetes.

"You can never miss a single day of treatment, and yet it's still not enough," Kramer-Golinkoff says. "It's really soul crushing, I'm in my 40s using oxygen and seeing my health deteriorate before my eyes."

Cystic fibrosis is a genetic, inherited condition causing thick and sticky mucus to clog vital organs, especially the lungs. Severe breathing problems typically follow, along with respiratory infections and malnutrition. CF gets worse over time and requires daily care, but many people are able to live full lives.

Modern day treatments have been lifesaving for many CF patients. But a small remaining percentage — which includes Kramer-Golinkoff — have not seen those benefits. Instead of accepting the limits of the moment, she helped create a way to push past them.

Patients left behind

"[Treatment] is getting more complicated," says Dr. Ahmet Uluer, the director of the adult cystic fibrosis program at Boston Children's Hospital. "More drugs are available, lots of drug interactions, so we need a lot of people — all hands on deck — to properly take care of somebody."

That shift in treatments has been lifesaving for many CF patients. One major advance is a class of drugs known as cystic fibrosis transmembrane regulator (CFTR) modulators, which help the CFTR protein work better in some people. But they are not an option for everyone, including patients whose genetics make them ineligible or whose bodies do not respond well enough.

"We really need to focus on those people who don't have modulator access," Uluer says. "People look at CF and say 'Your life is so great, everything's cured,' meanwhile in the hospital there are people fighting for their lives."

Enter: Emily's Entourage. Started in Kramer-Golinkoff's living room in 2011, it's since ballooned into a multimillion-dollar fundraising machine dedicated to those still waiting for effective options.

"Emily's Entourage focuses on those that don't benefit from existing CFTR modulators, whether that's due to ineligible genetic mutations, side effects from modulators, or suboptimal responses to CFTR modulators," Kramer-Golinkoff says. "For people who don't fall into those buckets, there's an organization singularly focused and fighting for them."

The nonprofit points to $22.1 million in support of lifesaving research and drug development, 42 awarded research projects to top investigators around the world, and over 353 developed phages that have treated 106 people with antibiotic-resistant infections, among its efforts.

> **"We strongly believe that people with CF should have information, access, power, and tools at their fingertips."**
>
> *Emily Kramer-Golinkoff*

But the story is bigger than one nonprofit. It is also a story about momentum, and about a region that keeps building the kind of infrastructure breakthroughs depend on.

New England's CF landscape

"Boston Children's is one of the biggest treatment centers in the nation," says Dr. David Waltz, chief medical officer at Emily's Entourage.

In Boston and across New England, CF patients can find physicians, nurses, nutritionists, respiratory therapists, and social workers working in concert at many accredited care centers.

"Basically every state in New England has a CF center," Waltz says. And for cystic fibrosis specifically, that rounded team of professionals is paramount. "The primary cause of morbidity and mortality is lung disease, but it affects all of the organ systems in the body. So you need a multidisciplinary team, and those are primarily found at those accredited CF centers here."

That clinical backbone matters for daily care. It also matters for what comes next. The same hospitals and research institutions that deliver long-term treatment help create the conditions for progress.

In this region, that work is increasingly complemented by biotech companies, like the ones featured in this section, pushing new lines of research and expanding the toolkit beyond today's standard therapies.

The future

The future of cystic fibrosis research is lit with optimism, but also clouded with some uncertainty. Funding will always be a looming obstacle, but Kramer-Golinkoff and the team at Emily's Entourage are pressing ahead.

"We have really ambitious, aggressive plans for funding," Kramer-Golinkoff says. "We're working closely with our grantees and collaborators to push to the finish line and to reverse-engineer solutions."

One effort that's near to Kramer-Golinkoff's heart was their development of CF Clinical Trial Connect, a global patient database to connect patients with relevant clinical trials — currently the only database of its kind. They reach out directly to patients, share with them what sort of resources and trials may be available, and connect them to the clinical trial site.

"We've supported about seven clinical trials now," Kramer-Golinkoff says. "We strongly believe that people with CF should have information, access, power, and tools at their fingertips."

With an urgency toward expanding patient access also comes excitement for the current treatment landscape, and what the burgeoning science could be capable of in the next few decades. Close collaborations between health care industry players and daring research projects are beacons of success across New England for the wider CF community. Still, the work is not finished for the patients who remain without effective options.

"The most promising things can get held up by huge hurdles, but having been in this space for 15 years, working closely with so many researchers on so many grants, we have a lot more insight to bring," Kramer-Golinkoff says. "At the end of the day, our superpower is our connection to the whole CF community and our understanding of how urgent every passing day is." ■

Kramer-Golinkoff smiles with her mother, Liza Kramer. Both are cofounders of Emily's Entourage.

Above, Kramer-Golinkoff demonstrates an airway clearance technique (ACT) .

Below, the Kramer-Golinkoff family joins together during the early days of Emily's Entourage.

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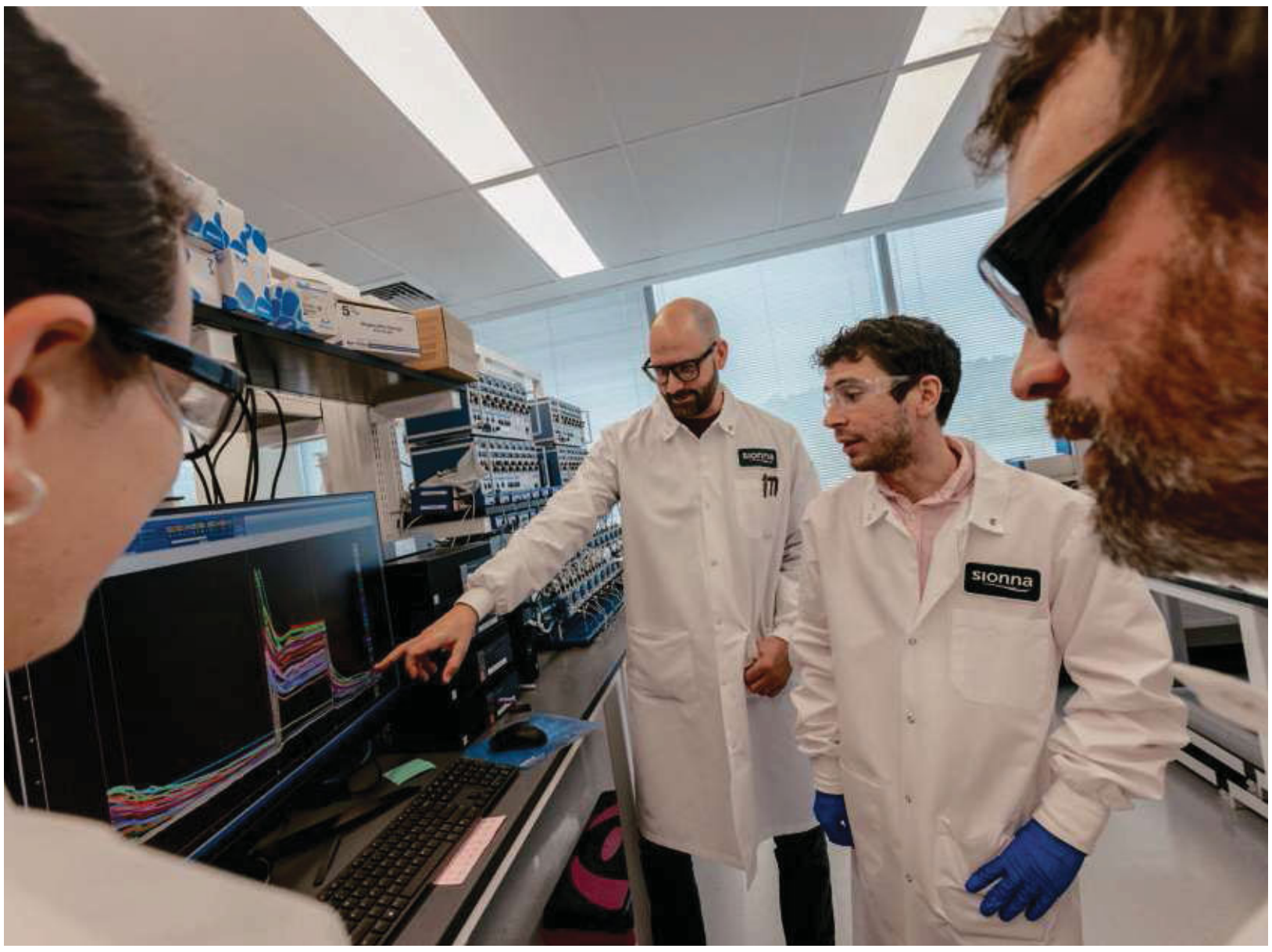

Scientists at Sionna examine results in their Massachusetts lab.

How collaboration drives progress in cystic fibrosis treatment

New approaches aim to advance treatment to further address unmet needs.

Provided by Sionna Therapeutics

For thousands of individuals and families living with the rare disease cystic fibrosis (CF) in the US, the impact is anything but rare. A generation ago, many children born with CF faced dramatically shortened life expectancy. Treatment was largely limited to managing symptoms, with a number of affected people ultimately requiring lung transplantation. Today, CF has become a powerful example of how scientific progress and strong advocacy can lead to meaningful change for people living with a serious disease. Sustained scientific investment, specialized care, and therapies that target the underlying drivers of the disease are helping people with CF live longer and healthier lives.

As the community marks CF Awareness Month in May, it is a moment to reflect on decades of scientific progress, and the collective efforts of people and families living with CF, researchers, clinicians, industry partners, and advocacy organizations such as the Cystic Fibrosis Foundation (CFF). Together, these efforts have strengthened the CF care ecosystem. It is a model for other rare disease communities seeking to champion improvements in care.

Even with meaningful advances in treatment, which have significantly improved the lives of people with CF, it remains a serious, life-threatening disease that continues to place a profound burden on those with the condition. Continued scientific innovation and collaboration across the CF community are essential to advance the next generation of therapies and address the unmet needs that persist.

Targeting the root cause of CF

CF is a rare genetic disease. There are approximately 40,000 children and adults in the US living with CF, with roughly 1,000 new diagnoses each year, per the CFF. Scientific discovery has deepened the understanding of the mechanisms of CF and has opened the door for the current suite of therapies that aim to target those underlying causes more effectively.

CF is caused by mutations in the gene that encodes the cystic fibrosis transmembrane regulator (CFTR) protein. This protein sits on the surface of cells lining organs such as the lungs, pancreas, digestive system, and sweat glands, where it regulates the movement of salt and water in and out of cells throughout the body. For CFTR to function properly, it must fold into the correct structure and move to the cell surface. In many cases of CF, genetic mutations disrupt this folding process, preventing the CFTR protein from working normally. The resulting imbalance of salt and water leads to the buildup of thick mucus and other secretions in multiple organs, contributing to serious complications such as chronic lung infections, breathing difficulties, and digestive issues.

The most common mutation that causes CF is F508del, which affects a critical part of the CFTR protein called the nucleotide-binding domain 1 (NBD1). NBD1 plays a key role in CFTR's folding, its movement to the cell's surface, and its overall function. For many years, researchers, including scientists at Sionna, have worked tirelessly to identify ways to target this region of the CFTR protein, believing that restoring stability to NBD1 could help correct CFTR folding and enable higher levels of CFTR function. However, NBD1 has proven to be one of the most challenging targets in CF drug discovery. While some currently available CF therapies, known as CFTR modulators, help improve CFTR function, no approved treatments directly target NBD1. Researchers at Sionna believe stabilizing NBD1 is central to unlocking dramatic improvements in clinical outcomes and quality of life for people with CF.

"At Sionna, we believe that progress isn't only measured in speed — it's about moving together. We believe progress will be possible when it's built side by side with the CF community, listening, asking questions, and learning from their experience."

Irene Aquino, senior director of patient advocacy at Sionna Therapeutics

A new approach to the next generation of CF treatment

Researchers at Sionna have made significant progress in addressing the longstanding challenges of targeting NBD1. The company is developing investigational therapies designed to directly stabilize this critical domain.

Building on more than 15 years of pioneering research, Sionna has identified novel molecules that can bind to and stabilize NBD1. In laboratory studies using established methods to assess CFTR activity, these molecules have demonstrated the potential to normalize CFTR function when combined with complementary modulators that target other regions of the protein. Sionna's NBD1 stabilizers are now being investigated in early human clinical trials.

Sionna's goal is to deliver differentiated CF medicines that have the potential to restore CFTR function to as close to normal as possible. Achieving that goal requires more than scientific innovation alone. Progress in CF has always been driven by a collaborative ecosystem.

"At Sionna, we believe that progress isn't only measured in speed — it's about moving together. We believe progress will be possible when it's built side by side with the CF community, listening, asking questions, and learning from their experience," says Irene Aquino, senior director of patient advocacy at Sionna Therapeutics.

Honoring the critical role of advocacy and community in CF

Patient advocates and organizations play an essential role in ensuring that the voices, experiences, and needs of people living with rare diseases are heard. CF Awareness Month offers an opportunity to recognize people with CF, their families, and the broader community whose dedication has shaped progress in research and care.

Over the past several decades, CF advocacy organizations around the world have been successful in raising awareness of the disease, while mobilizing resources to advance scientific discovery and improve clinical care.

A critical component of this success has been the community's commitment to supporting early-stage research. Organizations such as the CFF, along with other advocacy groups, have helped fund foundational scientific work and foster collaboration across academia, the industry, and clinicians. They also provide important guidance in the design and execution of clinical studies, helping ensure that development efforts reflect the needs and experiences of people living with CF.

Acknowledging that advances in treatment have helped many individuals with CF live longer, the work is far from finished. The next chapter of progress in CF will continue to be built in close partnership with the entire CF community — the families, clinicians, researchers, and advocates working together toward new treatment options for people with CF. ■

Brendan Sullivan, a person with cystic fibrosis, signs Sionna's commemorative beaker alongside Patient Advocacy Lead Irene Aquino, adding his message "Never Give Up" to inspire the community to keep advancing together.

Sionna Therapeutics CEO, CMO, and co-founders at the company's Massachusetts headquarters.

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A Boston biotech revolutionized the care of cystic fibrosis

Vertex's Chief Scientific Officer, Mark Bunnage, on the moon shot that worked, the patients still waiting, and what comes next in CF treatment.

Sponsored by Vertex Pharmaceuticals

For a child born with cystic fibrosis (CF) in 2000, the median predicted age of survival was 34 years, according to the Cystic Fibrosis Foundation. For a child born with CF in 2024, that number was 65. And for those who start therapies in adolescence, recent models project they'll reach their 80s.

Mark Bunnage, chief scientific officer at Vertex Pharmaceuticals, describes how treatment advances have expanded what many people with CF are able to consider. "People [with CF] now can be thinking about going to college, achieving other milestones in life," he says. "It's profound, meeting parents and children and people who have benefited from these therapies."

Vertex's five approved CF medicines can treat about 95 percent of people with the disease — and the company is not giving up on reaching the remaining 5 percent.

"When we started on this journey, we had this vision that we wanted to treat all people with CF," Bunnage says. "That's what we continue to try and do."

A quarter century of progress in CF

Cystic fibrosis is caused by inherited mutations in the *cystic fibrosis transmembrane conductance regulator (CFTR)* gene, which encodes a protein that regulates the movement of salt and water through cells. When the CFTR protein doesn't work as it should, thicker fluids cause damage to the lungs, digestive system, and other organs.

The path to treating the disease began with academic researchers who identified the *CFTR* variant as the root of CF and began mapping variants that cause the disease. Vertex built on that foundation by screening a million small molecules to see if they could fix the function of the mutant form of the protein.

"It was something of a moon shot project," Bunnage says. "Many people would think it would be next to impossible to do what we tried to do."

Years of optimization led to the 2012 approval of the first CF medicine to treat the underlying cause of the disease. Four more have followed.

Vertex credits those advances to a research philosophy it applies across every disease area: Commit to deeply understanding the biology at the root of the diseases, then attack from there.

"Our strategy is very distinct — this absolute, rigorous focus on human biology, deep understanding of the disease, human-based assays, and we'll use any tool in the toolbox," Bunnage says. The approach, which Vertex calls "modality agnostic," spans across small molecules and genetic therapies.

Reaching the patients still waiting

The company is working to extend its existing medicines to younger patients, including children and infants. "The sooner you could treat someone," Bunnage explains, "you're going to slow or perhaps prevent disease progression."

About 5,000 patients carry CFTR variants that produce no CFTR protein, leaving nothing for a small molecule to work on. For them, Vertex is pursuing genetic therapies designed to reintroduce the missing protein.

Vertex continues to invest in research beyond its own labs. Through the CF Research Innovation Awards, the company funds academic researchers continuing research in CF. Recipients are chosen by an independent panel that evaluates the proposals and allocates grants. "We are committed to ongoing research, not just our own research, but also from new investigators," Bunnage says.

Commitment that extends beyond medicine

Involvement in the CF community has shaped Vertex's program from the beginning, sometimes in ways that changed the science itself. Early in the project, a Vertex scientist attended a CF community event and noticed a white crust on another attendee's leather shoes. It was salt, a residue of sweat from a body whose chloride transport has gone haywire — the signature of CF.

"That was a moment when my colleague thought, 'You know what, we need to make sure we've got a systemic therapy for this disease because it's affecting the whole body,'" Bunnage says. That insight helped push Vertex toward an oral pill with the goal of treating CF across multiple affected organs, rather than the lungs alone.

Vertex has also invested in the CF community outside the lab — including a generation now planning for futures they once didn't expect to have. The Vertex Foundation has awarded more than 85 scholarships to people with CF or a family member pursuing college or advanced degrees. The company's Circle of Care grant is a global competitive grant opportunity that funds innovative patient-centric programs for the CF community. It has supported more than 100 participants in Team Impact, a nonprofit that pairs children with serious illness with college and high school sports teams, which helps foster a sense of belonging for the children.

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> *Mark Bunnage, chief scientific officer at Vertex Pharmaceuticals*

"These sorts of initiatives reiterate our commitment to helping meet the broader needs of the CF community," says Bunnage.

Why every day counts

When a Vertex medicine is approved, employees gather around a bell. Patients often join the occasion and share their stories before the bell is rung.

"There's not a dry eye in the house," Bunnage says, "because we know all that work to get our medicines to patients – sometimes many years of work, is why we do it. When you see that bell ring, it's all worth it."

What keeps him, and the scientists working alongside him, coming back regardless of the challenge is the people waiting beyond the lab.

"Every single day counts," Bunnage says. "People used to think having CF meant lung transplants as treatment. This may no longer be the case for patients who can potentially benefit from the right therapy."

In Vertex's Boston labs and around the globe, that pressure is what keeps the benches full — and the bell, eventually, ringing again. ■

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