Patient-Led Listening Session for the “Final 10%” of People With Cystic Fibrosis

July 15, 2021

Emily’s Entourage held a “Patient Listening Session” with the U.S. Food and Drug Administration (FDA) to advocate on behalf of the final 10% of the cystic fibrosis (CF) community that does not benefit from existing CFTR modulator therapies. The final 10% consists of people who do not benefit from the currently available CFTR modulator therapies due to ineligible mutations, side effects, or lack of access.

EMILY'S ENTOURAGE

Objective of Session

- Educate FDA staff about the final 10% of the cystic fibrosis (CF) community that does not benefit from existing CFTR modulator therapies and the urgent unmet treatment needs that remain.
- Build a strong, enduring relationship with the FDA.
- Ensure the perspectives of people with CF and their loved ones are included at every stage of drug development and approval.

Summary of Topics Discussed

- **Lack of a therapy to address the underlying cause for the final 10% of people with CF that do not benefit from a CFTR modulator.**
    - Significant progress has been made for 90% of people with cystic fibrosis who have access to highly effective CFTR modulator therapies targeting the basic, genetic defect of their disease. For those with the genetic mutations that these therapies treat, the drugs have been transformational, marked by a significant increase in lung function, decrease in salt chloride, weight gain, improved quality of life, as well as other critical health outcomes.
    - For the remaining 10% of the CF community that does not benefit from CFTR modulator therapies, CF remains the same progressive, deadly disease it has always been. There are urgent, unmet treatment needs that remain for novel genetic and transformative approaches to address the underlying cause of CF, as well as treatments that address common issues like infections and antibiotics resistance, which could help stave off the progression of the disease and achieve stability while they wait for their game-changing therapies.
    - In an anecdote shared by one of the community participants — a CF clinician — five of her patients were listed for a lung transplant; of those five patients, three became eligible for CFTR modulators and their health improved so dramatically that they were removed from the transplant list and remain off the transplant list to this day. The remaining two patients were not eligible for modulators and both underwent transplants, highlighting the significant divergence in health outcomes among those who benefit from modulators and those who do not.

- **CF significantly impacts multiple organ systems in addition to the lungs.**
    - Although primarily thought of as a lung disease, CF is an unrelenting, systemic, genetic disease that impacts the whole body and presents differently in every person with CF. In addition to the lungs, CF ravages the digestive tract, pancreas, sinuses, kidneys, liver, and more.
    - As the disease progresses, so does the need for additional treatments and care, placing a significant toll on the individual with the disease and their family members and caregivers. In a survey of more than 420 people with CF who do not benefit from existing CFTR modulators, conducted by Emily's Entourage in

June 2021, respondents reported doing an average of 4.8 non-pulmonary, CF-related treatments per day. (This is in addition to the pulmonary-related treatments required to manage their disease.)

- **Impact of CF on individuals with CF and their caregivers.**
    - The impact of CF on people's everyday lives is exorbitant. In the recent survey, 85% of respondents reported that CF moderately to significantly impacts their daily life, and 54% reported feeling isolated or like a burden to others. Sixty-nine percent of survey respondents reported having had at least one hospital stay in the year prior to COVID-19, and 14% had five or more hospital stays that year.
    - Several of the speakers mentioned difficulties maintaining gainful employment due to the uncertainty of their CF and shared the burden it has placed on their relationships. One speaker shared that the intense, progressive nature of CF robbed her of her teaching career, her marriage, and her dreams of having a family. Another speaker shared the crippling anxiety that CF has caused him, detailing his fears of not being able to breathe, that his lungs will eventually lose their function, and that he will end up in the hospital.
    - The impact of CF also extends to the entire family. In the survey, over 57% of caregivers reported that CF has a "significant impact" on their daily life, with 67% saying it impacts their mental health and 40% saying it impacts their physical health. One caregiver shared that the years since his daughter's diagnosis have been a whirlwind and that he is "scared beyond words" for her.

- **Time-intensive and burdensome nature of currently available treatments.**
    - In the recent survey, 40% of respondents said they spend at least two hours per day on routine medical treatments and, on average, survey respondents reported doing more than five pulmonary-related treatments (in addition to the aforementioned 4.8 non-pulmonary, CF-related treatments). One speaker shared her lengthy treatment schedule on an average day, calling it "grueling and relentless in terms of hours, energy, and sacrifices, not to say anything of the mental fortitude it requires." A caregiver shared similar sentiments as he spoke about his daughter's daily treatment regimen, adding that the frequency of her treatments increases to every four hours when she catches a cold.

- **Eagerness to participate in clinical trials.**
    - The CF community realizes that their hope for better futures and new treatments lies in clinical trials — and they are well-organized and eager to participate.
    - Of those surveyed, 77% said they are interested in participating in clinical trials, and 54% said they would be willing to participate even in the face of potential health risks as long as the possible benefits outweigh that risk. They understand that there is an unavoidable risk of not finding new treatments and CF does not stand still.
    - According to 37.76% of respondents, the main reason they have not participated in trials is because they did not qualify.

- **Desperation to share in the progress that has been realized for 90% of people with CF.**
    - Participants shared their happiness for those in the community who can benefit from the currently available CFTR modulator therapies and expressed their desperation to share in the progress too. They shared their fear of being left behind. One survey respondent said, “It feels good but terrible at the same time. I feel forgotten about in all honesty.” Another referred to the “have and have nots” in CF care now. One of the speakers said he is glad that this daughter is “not old enough yet to be crushed by the agonizing fear and frustration of realizing that you have nothing available to make you better when so many others are cheering incredible progress.”
    - They also mourned everything that CF has robbed them of thus far. One speaker said she dreams of having the energy to work full-time, travel, and experience things like her peers do. She wishes to be able to exercise, skate, ski, bike, and run without worrying. Another speaker said he feels like CF has made him live a life of fear rather than allowing him to be curious, explore the world, and take on new opportunities. A caregiver of a daughter who passed away from CF said she “would have traded everything for the chance to take a breath that didn't hurt … to have a life that wasn't defined by illness.”
    - Many CF community members noted the pressure of time they feel given the progressive nature of their diseases. They shared their hopes of one day benefiting from a breakthrough drug like their peers and their fears that it might not come in time.

Summary of Speaker Testimonials

See below under the “CF Community Testimonials” section.

Summary of Q&A

Following the speakers’ remarks, a Q&A session commenced, with members of the FDA asking questions of the panelists in the virtual meeting.

Q: If you had to pick one thing that you could improve, what would it be? There’s a myriad of issues you face, but what would the most important thing be to you? - Member of the patient affairs team at the FDA

- The mother of an adult with CF who passed away implored the FDA to consider phage therapy. She feels it is an important option to have for people with CF who do not have time to waste.
- An adult with CF said they need as many treatment options as possible, as everyone’s disease is so different. Specifically, treatments that are available for lung infections are

important. They need to stay healthy enough where they will be able to benefit from future transformational therapies.

- Another adult with CF agreed that it is important to have any therapies that could halt the decline of lung function. She said she would happily live with her current lung function of 38% if there was a way to make sure it would not go down further.
- An adult with CF, who shared that she has 35% lung function, said there is an urgent need for anti-infectives. When your lung function gets low, it sets off a cascade of problems, including lung bleeds and lung collapses. Small boosts in lung function can have huge effects in letting people with CF live a life less interrupted by their disease. The chance for stability is a gift.
- A sibling of an adult with CF, speaking on behalf of her sister, said she would appreciate anything that could reduce the amount of time spent on disease management so that she could maximize her quality of life.

Q: How has the pandemic affected you in terms of the treatment and care you are receiving? - Chat message from a member of the FDA, delivered by a member of the patient affairs team

- A father of a child with CF said it has made it easier for them to manage his daughter's treatments when she is sick. Prior to COVID, they would have had to take her out of school. This way, she was able to keep up with her class thanks to virtual learning via Zoom. The enhanced infection prevention and control measures that the school implemented have also been a help.
- An adult with CF said it has been interesting in terms of continuity of care during the pandemic. Her provider started doing virtual visits, and she is nervous about going back to the doctor in person again, as there are now psychological hurdles to overcome. She is still concerned about getting COVID, given her CF. She shared there has also been some emotional relief because the rest of the world is going through what those with cystic fibrosis go through on a daily basis. For example, worrying if a cold will land her in the hospital.
- Another adult with CF said, for her, there have been pluses and minuses. She has more time to do treatments and there are more opportunities to join events virtually, but she has also faced difficulties receiving treatment-related items via mail.
- An adult with CF said she was petrified for the first six months of the pandemic. Initially, she was concerned she might get sick with a CF issue and not have access to a hospital or ventilator. The "haves" and the "have nots" were also exacerbated during the pandemic, as most of the statistics that show people with CF fairing better from COVID than expected are for individuals on CFTR modulator therapies and do not represent the risks for those not benefitting from modulators. She remains in strict isolation today.

Q: What level of side effects would you be willing to accept or not willing to accept in a treatment? Are there any examples of times where you stopped treatment? - Member of the orphan products development team at the FDA

- A father of a child with CF said they do not have any treatments available that address the underlying cause of his daughter's CF. The only treatments currently available to her

are burdensome, time-consuming daily treatments that address the symptoms, rather than correct the underlying genetic defect of her disease. If it meant extending her life, they would be willing to pursue any opportunity as long as the risks did not put her life in unnecessary danger. There would be a lot they would tolerate before they would say no.

- An adult with CF agreed, saying it is all about value, which shifts as your disease progresses and you run out of treatment options. There is a lot she would and does endure. The side effects that have made her come off drugs are when the side effects are life-threatening (i.e. lung bleeds). There are very few things that would keep her from something that provides value. A lot of medications make her sick and she finds creative ways to endure, for example taking medications that make her sick to her stomach with crackers, because she is desperate and beggars cannot be choosers.
- The mother of an adult with CF who passed away mentioned a specific clinical trial that enabled her daughter to gain weight and experience an increase in lung function, but failed to meet the clinical trial endpoints. She feels that when a person is at the end-stage of a disease, there should be more consideration given to treatment options and pain management. In her daughter's instance, doctors were strict around pain management because of the opioid epidemic, but she felt there should have been different considerations given her health status.

Key Takeaways

Following the Q&A session, Emily Kramer-Golinkoff, co-founder of Emily's Entourage, shared the following key takeaways.

- **CF is not done.**
    - This urgent quest is far from over — not for the 90% of people with CF who are currently eligible for CFTR modulator therapies, but especially not for those with CF in the final 10% that do not benefit from modulators. They are still contending with the same killer disease that CF has always been.

- **For people with CF who have untreatable mutations, the status quo is fraught with danger.**
    - Many in the final 10% are willing to accept risks when it comes to potential new treatments because the alternative is suffering and untimely death due to this disease. If given the opportunity, many people with CF would choose to take the risk of a new treatment, or potential risk in the future, in return for the time they may otherwise never have.

- **Breakaway successes — like some of the current CFTR modulators — and forever cures are the dream, but buying time and achieving stability alone are huge wins for the final 10%.**
    - The natural course of CF is progressive. Without treatments to halt its natural trajectory, individuals with CF will continue to lose critical lung function and

contend with worsening side effects of CF with each passing year. Achieving stability and even modest increases in function reflect significant advances in treatment and translate to major improvements in health and quality of life for those with CF.

- **Timing and speed are everything.**
    - With a progressive disease that resists even the most valiant attempts at control, years, months, and weeks matter. At the end of the day, time equals lives. The CF community urges the FDA to prioritize drug reviews and apply regulatory flexibility for people for whom waiting might be the difference between life or death.

- **The impact of CF runs deep. It ravages the lungs, digestive tract, pancreas, sinuses, kidneys, liver, and more.**
    - The herculean act of enduring — of working so hard to stay on top of treatments and slow the progression of the disease — has enormous impacts on the mental health of people with CF, as well as the mental and physical health of their families and caregivers. They work so hard every day to stay on top of their treatments and slow the progression of the disease, but it is not enough. They need help.

CF Community Testimonials

Six members of the CF community shared their experiences living with the disease. The community members represented a wide range of disease stages, manifestations, ages, ethnicities, gender identities, and more, which reflect the diversity that exists within the CF community and especially within the final 10%. Below are summaries of their testimonials, which included the experiences of three individuals with CF and three family members of individuals with CF.

Participant #1 (an adult with CF whose testimonial was read by her sister). The individual was diagnosed with CF within 24 hours of being born due to an intestinal blockage common among infants with CF. For the next 24 hours, she fought for her life due to a perforated intestine and rupture, requiring an emergency ileostomy. Her parents were told she wouldn't survive, but she defied the odds and made it through.

She started becoming sick more frequently in middle school, fighting sinus and lung infections that seemingly never ended. Her disease progressed during high school when she contracted Burkholderia cepacia, a relentless bacteria that caused recurring infections to her lungs. No amount of treatments could prevent the recurrent lung exacerbations. Eventually she became tethered to oxygen concentrators 24 hours a day and IV antibiotics around the clock, in addition to taking dozens of pills each day.

She earned a master's degree in education, but after only three years of teaching, the progressive nature of her disease forced her to quit and apply for disability and Medicare. Her tenure was marked with health episodes, including one where she woke up in an ambulance, completely numb and paralyzed with blood covering her face and chest. In addition to her career, her marriage also ended due to the intense nature of her disease.

In the past five years, she has continued to endure similar episodes accompanied by stroke-like symptoms and suffers from PTSD as a result. She is recovering from a double-lung transplant, which she viewed as her last-ditch effort to breathe and is why her sister read her remarks in her place. She thinks a lot about how different her life could have been if she had been eligible for a CFTR modulator therapy, hearing and seeing how it is benefiting others. She doesn't want to be left behind.

Participant #2 (father of a child with CF). The participant's daughter was diagnosed with CF through newborn screening. Not only had he and his wife never heard of CF, but they had done genetic testing when they learned they were pregnant, and the test came back with results that determined they were not carriers of CF. Upon their daughter's diagnosis, they were quickly thrust into the whirlwind world of health care, medicine, and rare disease.

Their lives have changed dramatically in the past seven years. His daughter starts her mornings with medicine to open her lungs and break up the mucus, which she inhales through a nebulizer, and an airway clearance technique using an inflatable vest that shakes her body to loosen the mucus in her lungs. Before bed, she must complete this entire pattern for the second time in a day. All of this is when she is healthy. If she catches a cold or the flu, then this exercise is repeated every four hours.

For his daughter's genetic mutation, there is no CFTR modulator therapy available. The new advancements in CF mean absolutely nothing for her. In a way, he and his wife are glad that she is not yet old enough to realize that she has nothing available to make her better.

They do not have the luxury of waiting for decades for multiple studies due to the unrelenting, progressive nature of CF and they are open to wide-ranging opportunities for research participation. They understand that there are risks involved with any new breakthroughs. If they felt, in consultation with their daughter's doctors, that death or permanent damage was unlikely (less than 1%), they would likely participate in a trial.

Phage therapy, mRNA, Crispr, and many other emerging technologies all hold tremendous promise. They would especially embrace studies around gene therapies, whether the host DNA is altered or a temporary mRNA molecule is introduced. They understand statistics and can talk things through with their daughter's care team.

He shared that his daughter has much to offer the world and he is honored to be her father. At the same time, he is scared beyond words. She is his only child, and the thought and fear of losing her is something that he cannot even begin to describe.

Participant #3 (adult with CF). The participant was diagnosed with CF at two-and-a-half years old after facing recurring respiratory infections and frequent hospital stays requiring an oxygen tent. Her journey to diagnosis was longer due to inconclusive test results and a Hispanic descent, which led doctors to believe she couldn't have had CF. Thanks to her family's persistence and a pediatrician who advocated on her behalf, she received a proper diagnosis.

Growing up, she missed a lot of school as she combatted respiratory and sinus infections, falling off the growth curve and narrowly avoiding a feeding tube. At 15, she required two PICC lines because of her frequent respiratory infections and suffered many medical complications and side effects that resulted in lasting mental trauma. Growing up, she did her best to stay active but always found it challenging to keep up with her peers.

In a professional setting, she finds it difficult to meet the same expectations as her peers because of her medical needs. She spoke to the intense treatment burden of her disease, which is time-consuming and leaves her feeling exhausted.

Cystic fibrosis requires daily medical treatments that she cannot miss, so she lugs her 20-pound vest around that helps break up mucus in her lungs. As an adult, she is motivated to complete all of her daily treatments because she knows that she does not have many treatment options left, having already exhausted several of the treatment options available to her. She hopes to stay off the lung transplant list, the only remaining treatment option for individuals with end-stage cystic fibrosis, for as long as possible.

Seeing her friends with CF who have access to CFTR modulators makes her happy, but also envious. She dreams of having the energy to work full-time, go to events with others, travel around the world, and explore and experience things like her peers do. She wishes to be able to exercise, skate, ski, bike, and run without worrying and having to think in advance of all the things she needs to prepare. She hopes to have a breakthrough drug so she does not have to ultimately rely on a lung transplant to survive.

Participant #4 (adult with CF). The participant was diagnosed with CF at a young age and remembers doing airway clearance treatments as a toddler. In elementary school, he didn't think much of his CF other than feeling frustrated that he had to miss time playing basketball with his friends to go to the office to take his enzymes before eating lunch, getting called out of class to take antibiotics, and being pulled from school for CF appointments.

In high school, he became more aware of the hardships associated with living with CF, missing school due to infections that required extra rounds of airway clearance and added medications.

The most painful part of CF to him is the hospitalizations, of which he's had many. Within his first quarter of college as a neuroscience major, he was hospitalized twice: once in November for eight days and again in December for an entire month. The worst part of the hospital to him is the agonizing uncertainty of how long he will be there and the social anxiety when he's stuck in the same room for days on end.

He tries to tell himself that his health will go back to where it was, but deep down he knows that it won't be the same. He spoke to the treatment burden and the frustration that even after hours of treatments, his lungs still don't feel great and his lung function continues to decline. There are many times when he brings up so much phlegm due to coughing that he has to lay down and rest, which takes away time from his schoolwork, hobbies, and spending time with friends.

More than the physical aspect of CF, it has taken a toll on his mental health, making him feel worried for the future. He gets anxiety that he can't breathe, that he'll end up in the hospital, and that his lungs will eventually lose their function. He feels that he's lived a life of fear, rather than allowing himself to be curious, explore the world, and take on new opportunities. He hopes for a drug that not only could relieve the coughing and other painful symptoms of CF, but also reduce the number of treatments and medications that he takes on a daily basis. He wants to be able to live a life where he can relax and focus on what's around him rather than living the life of fear he currently experiences.

Participant #5 (parent of an adult with CF who has passed away). The participant's daughter passed away from CF in 2017 at 25 years old, just two months after receiving a double-lung transplant. She shared that her heart breaks that her daughter did not get to benefit from any of the CFTR modulator therapies that are now available to 90% of people with CF, and she hopes others in the final 10% will have a better outcome.

Her daughter was diagnosed with CF at three years old due to a persistent cough, chronic runny nose, and serious GI problems. Her doctors started her on treatment the day after she was diagnosed.

As a toddler, she hated doing the treatments. Every day when it was time to start, she would hide anywhere she thought her parents would not find her. It was unbearable for everyone. Eventually, she got used to it all and had a very happy childhood. She was always compliant until one day at the age of nine, she refused to do treatments anymore. That is when her parents introduced the idea that CF could be fatal and explained that was why she had to follow such strict treatment protocols. She cried for three days but then seemed to accept that her life was different.

When she was 12, she came home from camp very sick and had her first hospitalization, the result of an aggressive Burkholderia cepacia infection. Treatments got more complicated and life got harder.

Having CF forced her to straddle the line between the sick and the well worlds and complicated her normal childhood development. Doing lengthy treatments two to four times a day was disruptive academically and socially, and yet she was a straight-A student, three-sport varsity athlete, and a beloved friend and family member to so many.

For most of her life, CF was invisible, so everyone thought she was the golden girl who had it all, but she would have given anything for the chance to have a life that was not defined by illness. She was often worried about her disease and what life would bring. To manage her anxiety, she spent time in nature whenever possible and wrote her college thesis in parallel stories comparing the slow destruction of the Hawaiian ecosystems with her declining lung function from a superbug.

When she spoke at her college graduation, she quoted Winnie the Pooh: “I used to believe in forever … but forever was too good to be true.” In one of the last conversations with her mother, prior to passing away from cystic fibrosis, she wrote, “CF is a complex, unpredictable, irreversible, progressive, painful, suffocating, choking weed of a disease and it’s okay to hate it.”

Participant #6 (an adult with CF). The participant was tested for and diagnosed with CF at birth in 1977 after her older brother was diagnosed with CF. Her parents had not known what CF was prior to her brother’s diagnosis and were told by doctors that having another child with the disease would be virtually impossible.

On good days, when she is stable, she spends approximately three hours per day doing breathing treatments, sinus rinses, and airway clearance. The labor CF demands is grueling and relentless in terms of hours, energy, and sacrifices, not to say anything of the mental fortitude it requires.

The impact on her life has been far-reaching. She has never been able to hold a full-time job and has lost friends, missed many events and gatherings, and has turned down many travel opportunities. Decisions, from the smallest daily choices like whether or not to meet a friend for brunch, to significant, life-altering ones, like whether or not to move across the country, require complicated risk assessments. The older she gets and the more the disease progresses, the easier it feels to simply say no. Some days just speaking requires more energy than she has.

Growing up, she never let herself imagine a future beyond a couple of years, and she certainly never imagined a future in which she would become a mother. But at 24, she gave birth to her daughter and was bestowed with the greatest gift and responsibility of her life. Her mandate became staying as healthy and strong as possible for as long as possible so she could raise her child. Throughout her daughter’s life, she hoped to reach different milestones. Today, with transplant and quality of life discussions occurring with her doctor and family, she hopes to make it two more years to watch her daughter graduate from college.

She has witnessed the power of drug approvals firsthand. When a new antibiotic was approved in 2010, she started it immediately. She regained lung function and was able to avoid hospitalizations for several years. Those years of stability and uninterrupted time with her daughter were an enormous gift for which she will forever be grateful. She asked the FDA to help her buy more time so she can keep holding her daughter's hand.

Partner Organizations

- Cystic Fibrosis Research Institute (CFRI)
- Hyman, Phelps & McNamara, PC

Emily's Entourage would also like to thank the countless other individuals and groups in the CF community that have shared their stories and insights with the organization on an ongoing basis.

FDA Divisions Represented

- **Office of the Commissioner (OC) – *5 offices***
  - OC/OCPP/PAS - Office of Clinical Policy and Programs/Office of Patient Affairs *(organizer)*
  - OC/OCPP - Office of Clinical Policy and Programs
  - OC/OCPP/OCP - Office of Clinical Policy and Programs/ Office of Clinical Policy
  - OC/OCPP/OOPD - Office of Clinical Policy and Programs/Office of Orphan Products Development
  - OC/OCPP/OPT - Office of Clinical Policy and Programs/Office of Pediatric Therapeutics

- **Center for Biologics Evaluation & Research (CBER) –2 *offices/divisions***
  - CBER/OCD - Office of the Center Director
  - CBER/OCBQ/DIS/PSB - Office of Compliance and Biologics Quality/Division of Inspections and Surveillance/Program Surveillance Branch

- **Center for Devices and Radiological Health – *1 office***
  - CDRH/OSPTI/DAHRSSP - Office of Strategic Partnerships and Technology Innovation/Division of All Hazards Response, Science and Strategic Partnerships

- **Center for Drug Evaluation and Research (CDER) – *6 offices/divisions***
  - CDER/OCD/PASES - Office of Center Director/Professional Affairs and Stakeholder Engagement Staff
  - CDER/OND/ORPURM/DRDMG - Office of New Drugs/Office of Rare Diseases, Pediatrics, Urologic and Reproductive Medicine/ Division of Rare Diseases and Medical Genetics

- CDER/OND/ORPURM/DRDMG/DPMH - Division of Pediatrics and Maternal Health
- CDER/OND/ON/DNI - Office of New Drugs/Office of Neurology/Division of Neurology I
- CDER/OTS/OB/DBI - Division of Biometrics I
- CDER/OTS/OCP/DTPM - Office of Translational Sciences/Office of Clinical Pharmacology (OCP)/Division of Translational & Precision Medicine

Disclaimer

Discussions in FDA Rare Disease Listening Sessions are informal. All opinions, recommendations, and proposals are unofficial and nonbinding on FDA and all other participants. This report reflects the [organization]'s account of the perspectives of patients and caregivers who participated in the Rare Disease Listening Session with the FDA. To the extent possible, the terms used in this summary to describe specific manifestations of [disease or condition], health effects and impacts, and treatment experiences, reflect those of the participants. This report is not meant to be representative of the views and experiences of the entire [disease or condition] patient population or any specific group of individuals or entities. There may be experiences that are not mentioned in this report.