Targeting the Toughest Diseases

Episode 1 – Cystic Fibrosis Script

Boomer Esiason: *Well, I was getting ready to step on the field for the New York Jets for the first time in 1993.*

NFL quarterback Boomer Esiason had just been traded to the Jets after ten incredibly successful seasons with the Cincinnati Bengals. A team where he'd racked up a Super Bowl appearance and an MVP award.

He was born and raised in New York – so it was exciting to play for one of his hometown teams. But then, just as he was about to walk onto the field, he was called back.

Boomer Esiason: *The head coach's secretary came out onto the field and said, your wife is on the phone. You need to take the phone call. So, I took the phone call.*

It was Boomer's wife Cheryl, who was back in Cincinnati with their son, Gunnar.

Boomer Esiason: *Cheryl told me I needed to get back to Cincinnati, that Gunnar was in Cincinnati's Children's Hospital, and he was having trouble breathing.*

Boomer grabbed the next flight to Cincinnati, then went straight from the airport to the hospital.

Boomer Esiason: *Seeing a two-year-old Gunnar laying in a crib hooked up to all sorts of different machines, receiving antibiotics, was on oxygen. And I really wasn't sure what to think.*

The doctor came into the room and told Boomer and Cheryl that their little boy had cystic fibrosis.

Boomer Esiason: *That day will live with me forever as one of the saddest days of my life.*

Hi. I'm Jordan Gass-Pooré, I'm a member of the University of Southern California's Center for Health Journalism.

This is *Targeting the Toughest Diseases*, a podcast produced by Bloomberg Media Studios and Vertex Pharmaceuticals.

In this series, we look at some of humanity's most challenging diseases, and how Vertex – a Boston-based biotech company – is using innovative tools, methods, and a unique philosophy to search for treatments and cures.

Today, we're looking at cystic fibrosis, also known as CF, a rare, chronic, genetic disease affecting the lungs and other organs. It can lead to all sorts of complications, including lung disease, liver disease, diabetes, and even premature death.

It affects about 30,000 Americans and more than 80,000 people globally, making it a disease not a lot of people know about.

But it was not new to Boomer Esiason:

Boomer Esiason: *Here's the really weird part of this and maybe the destiny and irony part of all of this. Back in 1989, I was receiving an award as the best quarterback in the NFL. And at that awards banquet, there was a speaker that night because there was a fundraising attachment to that banquet. And his name was Frank Deford.*

Deford was a legendary writer at Sports Illustrated, but he was also a CF Dad.

Boomer Esiason: *Frank spoke so eloquently about how he lost his daughter Alex to the disease of cystic fibrosis which I had never heard of. She was eight years old, and everybody was captured by his story that night. I was very captured. I was crying.*

Boomer Esiason was 27 at the time with no kids of his own. He was living a great life as an NFL quarterback. But something in that speech touched him deeply. He asked Deford how he could help.

Boomer Esiason: *And he said, well, if you go back to Cincinnati and you can get involved in some of the fundraising aspects of cystic fibrosis, you know, put a face on it, if you will, and then maybe visit some of the kids at Children's Hospital, that would really be helpful.*

And that's exactly what he did. He used his celebrity status to help raise awareness and funds for cystic fibrosis, and he visited kids in the hospital who were sick.

Now his son Gunnar had this same, terrible disease.

We all have mucus that lines our lungs and our airways. This mucus has an important job. It captures dust and germs in the air we breathe. When mucus traps those germs and dust, tiny little hairs on the outside of our cells called cilia push all that mucus out of our lungs.

Normally, this mucus is slippery and watery. But for people with cystic fibrosis, this mucus is sticky and thick. As a result, the cilia can't push the mucus out and it ends up blocking lung passages, making it hard to breathe. Also, germs and bacteria get trapped in a person's airways making them more prone to infections.

Clearing the mucus could be a daily task for people with CF. There are medications that help thin it. Some patients use a vibrating vest to literally shake the mucus out of their airways. Others may have to visit the hospital periodically for a cleanout.

And because the mucus can also block the ducts to the pancreas – many people with CF may struggle to absorb nutrients efficiently. Solving that can require periodic IV treatments or taking enzymes to help breakdown food for absorption. IV treatments are also used to fight frequent infections in lungs that come about in many people with CF.

It's a demanding regiment. Something Gunnar Esiason had to confront when he was still very young.

Gunnar Esiason: *My dad who was driving the car. Just looked at me while we were driving and said, 'Gunnar, this isn't gonna hurt.' And for the entire rest of the car ride, he continued to say, 'This isn't gonna hurt, this isn't gonna hurt, this isn't gonna hurt.' As if he was reassuring me about something they weren't telling me about.*

Everything was fine – until the moment Gunnar realized the antibiotic treatment he was getting for a CF-related infection involved needles.

Gunnar Esiason: *I looked at my dad square in the eye. I said, you lied to me. And I ran out the door, down the hallway and into the lobby of Cincinnati Children's Hospital. So, if you can picture the scenario: There's my dad, the starting quarterback of the Cincinnati Bengals at the time chasing his belligerent child, and he finally comes up to me and he is like, 'Quiet, please be quiet. You're making a scene. I will do whatever you want if you go back into that room with me.'*

Eventually, after a lot of persuasion – Boomer agreed to buy Gunnar a video game console if he would go and get the treatment.

Gunnar Esiason: *So, we walked back into interventional radiology, and they strapped me down to the table, and I cried and screamed through the entire thing. But you better believe it that I got my Nintendo at the end of that hospital visit.*

In college, Gunnar reached a turning point with how he coexisted with the disease.

Gunnar Esiason: *My senior year was a real slog. Like I went through like several bouts of pneumonia. I knew that I was at a point in my life where, I had no other options.*

That uncertainty. Having big questions about the future is one of the hardest parts of living with CF.

Cystic fibrosis is genetic.

Our genes give our cells instructions on how to produce certain proteins. They tell the cells in our lungs, pancreas or sweat glands to make a special protein called cystic fibrosis transmembrane conductance regulator – or CFTR for short. This CFTR protein is sent to the surface of a cell. Here, it acts like little channels between the inside and the outside of a cell.

These channels open and close, and this allows particles like chloride ions to move in or out of a cell. And those chloride ions help a cell maintain a healthy balance of salt and water.

But for people with CF, a mutation causes the gene to give faulty instructions to the body. Those proteins – those little channels – don't work right. This means water and salt can't flow freely in and out of a cell like they should.

When that chloride gets trapped in a cell, it doesn't have the fluids it needs to hydrate its surface properly. Without those fluids, mucus becomes dehydrated. And that's what causes it to be thick and sticky.

Dr. Chinedu Nwokoro is a pediatrician in London. He has spent decades researching the condition and says we've known about CF since ancient times.

Dr. Chinedu Nwokoro: *If you go back to European Proverbs, you may have heard, there was a saying 'Woe to that child which when kissed on the forehead tastes salty. He is bewitched and soon must die.'*

Salty skin is a symptom because people with cystic fibrosis have two to five times the normal amount of salt in their sweat.

Dr. Chinedu Nwokoro: *These old grandmothers in Northern Germany were describing children with cystic fibrosis.*

The genetic mutation that causes CF survived because it provides its carriers with some extra immunity.

Dr. Chinedu Nwokoro: *Having one copy of the cystic fibrosis mutation seems to protect against diarrheal diseases like cholera and typhoid. That would've meant that people who were carriers of that gene would be more likely to survive plagues of cholera and typhoid where people who didn't have any copies would've been more likely to succumb.*

It was 1938 that the disease was named and made it into medical literature. It was discovered in children who had died of malnutrition.

Dr. Chinedu Nwokoro: *The U.S. pathologist Dorothy Anderson found that their pancreases were damaged through being bunged up by sticky secretions. And they were cystic and fibrotic and that was the name given to the disease.*

Dr. Nwokoro says life expectancy for children living with CF has been extended thanks in large part to newborn screening and improved treatments. But he is hopeful that treatments will not just extend life for patients living with the disease, it will improve their quality of life as well.

Dr. Chinedu Nwokoro: *What I hope that will lead to is a reduction in the need for the kind of intense therapy, both in terms of antibiotics, hospital admissions and in even physiotherapy, that have been characteristic of cystic fibrosis care over the years.*

Coming up with therapies that can both *prolong* and *improve* life is a pretty tall order. But it's a passion for Dr. David Altshuler, Chief Scientific Officer at Vertex Pharmaceuticals. As a physician and a researcher, he's spent the last 35 years of his career scouring our DNA code for *clues* about some of the world's toughest diseases.

Dr. David Altshuler: *So, the first thing we do is we look for diseases with great unmet need. Where the disease is very serious, and people's lives are impacted. And there's nothing that really is transformational that can really change their lives, and cystic fibrosis certainly was that.*

The second was, we looked for a case where the underlying human biology, the underlying cause of the disease is known. And again, in CF, the cystic fibrosis gene mutation was known.

What was missing was therapeutics that could do what needed to be done, which is in this case, restore CF function. And that's the kind of thing that really gets our scientists and doctors fired up. And so, they worked on it for 20 years to get where we are today.

Jordan Gass-Pooré: *Can you speak a little bit more about how you and Vertex are tackling cystic fibrosis.*

Dr. David Altshuler: *So, the work that Vertex has done in CF really goes back decades. It ran in families… but until 1989, when that gene was cloned, no one actually knew what caused the disease.*

That changed with the discovery of CFTR.

Dr. David Altshuler: *But then the question was, could you repair it? And for a period of decades that seemed impossible. People tried lots of different things and couldn't figure it out. But 20 years or more ago, scientists at Vertex had an idea. They had an idea of how to use chemicals to coax the CFTR protein that's not working, to function again.*

That's what Vertex has been working on for the last 20 years, and now has approved medicines with the potential to treat up to 90% of all people with CF. And they're not done yet.

Dr. David Altshuler: *One of the things that keeps us working hard on this problem is that less than 10% don't make any of the protein.*

The way current therapies work is to coax the protein that has an inherited mutation to function again. But some people don't make any protein – so a different approach is needed.

Dr. David Altshuler: *And so, we have research ongoing in our laboratories and, with a number of partners, are working hard for the last 10%.*

We're still very much in the CF story. We still have a long way to go until we reach our goal.

For people with CF like Gunnar Esiason, things that once felt unimaginable, now seem possible.

Like returning to school to see old friends.

Gunnar Esiason: *I had my 5-year college reunion. And most people would remember me from my college days or my last, you know, year or two as being very very sick, like always missing things, missing social activities, missing class… missing things like that.*

Gunnar Esiason: *Yet here we are at this reunion and it's like, the chance to go back to college, right? And we are staying out late and the next thing you know I'm up every morning at like six-thirty getting breakfast for everyone. And my friends were like, 'what is going on with you?'*

But as great as the weekend was – the drive home with his girlfriend was even more impactful.

Gunnar Esiason: *We were stuck in the New Jersey turnpike, and she looked at me and she was like 'do you realize what we did this weekend? Like, we went away and were able to do something. What do you want to do next with your life?' And I paused for a moment, and it hadn't occurred to me that I could do something with my life. I didn't have to live at home anymore.*

What they decided to do next… was get married.

Boomer Esiason: *I've never been at a wedding where everybody, I mean, all 250 people just came together as one group and were crying and were laughing and cheering. And it was like the greatest moment of all of our lives.*

Going back to school… getting married… those experiences are possible because of one thing: Hope.

Boomer Esiason: *Well, I dunno how much of a football fan you are… but when you play for the Jets, Cardinals, and Bengals, it's all about hope. You need as much hope as you possibly can get.*

Gunnar Esiason: *You know, I think for me, I mean, honestly, hope is going define the rest of my career.*

Gunnar Esiason: *When I was going through the worst of it, had a little quote on my desk, and it was a Winston Churchill quote. And it was something like, if you're going through hell, keep going. And that meant a lot to me back then.*

This is *Targeting the Toughest Diseases* a podcast from Bloomberg Media Studios and Vertex Pharmaceuticals.

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I'm Jordan Gass-Pooré, thanks for listening.