Cardiovascular and Renal Drugs Advisory Committee; Notice of Meeting; Establishment of a Public Docket; Request for Comments—New Drug Application 215244 for Elamipretide Hydrochloride Injection

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Submissions from:

Community Member Submissions

Emily Allen

Community Member, EAP

To the U.S. Food and Drug Administration,

I'm writing to support the approval of Elamipretide for treating Barth Syndrome. My son, Arthur, was diagnosed with Barth shortly after birth, and at six months old, he had to undergo a heart transplant, which saved his life. However, Barth Syndrome is still something we face every day, beyond the heart issues.

Arthur was put on Elamipretide before his transplant, but unfortunately, he was taken off of it just days after his surgery. Even though we didn't have enough time to see the full results, I truly believe that the drug was helping him. I am confident that had he stayed on Elamipretide, it would have continued to benefit his growth, energy, and overall development. Barth Syndrome affects more than just the heart it impacts daily energy, growth, and quality of life and Elamipretide gave us hope that we could see improvements in these areas.

Even now, after the transplant, we continue to manage the effects of Barth, and I believe this drug could have been a crucial part of his ongoing care. I'm asking you to consider families like mine, who are always searching for better treatment options. Elamipretide has the potential to make a real difference, and approving it could give many children a better chance to grow and thrive despite their diagnosis.

Thank you for your time and consideration.

Sincerely, Emily Allen,Mom of Arthur

Josanne Archibald

Community Member, EAP

My name is Josanne Archibald, I am writing to you as both a parent of three boys with Barth Syndrome and as an advocate for children affected with Barth Syndrome, a rare, life-threatening, and debilitating genetic disorder. Three years ago, I wrote a letter to you asking that you consider reviewing Elamipretide for children with Barth Syndrome. Three years ago, the thought of a drug that had the ability to have a profound impact on the survival outcome of babies born with Barth Syndrome seemed promising at the time but also completely out of reach.

In my last letter I introduced you to my son's Elijah and Mason, I spoke about our near-death experience with Mason days after he was born, which lead to a lifesaving heart transplant at 6 weeks old. I also spoke about receiving the genetic results that showed both boys had Barth Syndrome. So much has changed since then and my understanding of the complexities of this disease has broadened. Elijah is now in college and Mason in third grade, and we now have a new addition Josiah, who was diagnosed prenatally with Barth Syndrome.

Barth Syndrome has been a constant source of fear and hardship for our family. My children have experienced dilated cardiomyopathy, skeletal muscle weakness, neutropenia, and an array of metabolic dysfunctions. It severely compromises the quality of their lives, often requiring frequent hospitalizations and constant medical care. For children like mine, the future is uncertain, and the daily toll of this disease leaves them unable to live the active, fulfilling lives every child deserves.

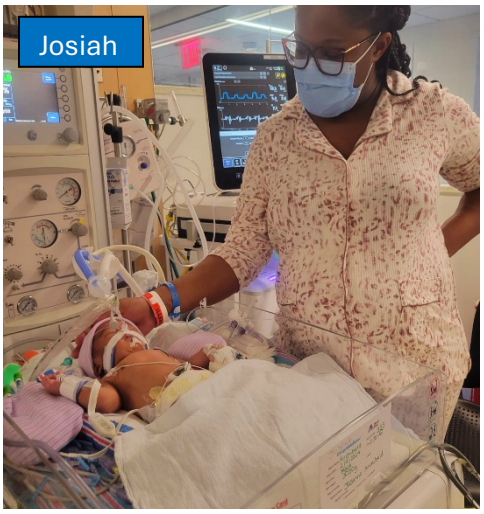
Barth Syndrome affects all my boys in different ways. For Elijah we struggled with weight gain, muscle weakness, growth delay and a complete intolerance to any physical activity. Elijah struggled with bullying in school due to his small frame and he could not enjoy his favorite sport, basketball, due to his muscle weakness and fatigue. This impacted him severely in an emotional and physical way. Elijah's struggles manifested themselves in High School where he was constantly injured in gym class or while playing basketball. His thin frame was the topic of conversation for the school nurse as she inquired about life at home and if we had enough food for our children. As a family we were determined to find options, so we spoke to Elijah's doctor about placing a G-tube to provide nutritional support and give him the chance to do the things he wanted to do. While the G-tube helped him gain weight and feel stronger it did not help with the fatigue and muscle weakness he felt after every activity. Elijah is now eighteen and has learned to accept his limitations and embrace a disease with which he must live. He is a well-rounded young man with a promising future in sport management.

Learning I was a carrier for this disease was very hard for me to accept. The why's were never answered so I found comfort in accepting that we do not choose our genetic makeup. Finding out you are pregnant should bring a sense of joy and overwhelming happiness, unfortunately this was not true for our family. The summer of 2023 was especially hard for our family when we found out that I was unexpectedly pregnant. The fear and uncertainty that flooded my mind in that moment is something I would not wish on anyone. The thought of bringing another child into the world to endure the same trails as my second son Mason was too much to bear. Josiah was diagnosed with amniocentesis and the news of his diagnoses was completely devastating. We prayed day and night for his health and prepared for the worst.

In my first letter, 3 years ago, I advocated for Elamipretide, and never would I have imagined that this same drug would be the center of my child's care. Preparing for Josiah was a mighty task. My very close connection with the Barth Syndrome community helped me create connections with my local doctors and the doctors doing the research for Barth. Josiah was born into a room filled with fifteen or more doctors, specialists, nurses, and a care team, ready to administer care. Josiah was born severely sick and needed immediate attention. Compared to when Mason was born, every doctor providing care to Josiah knew about Barth Syndrome and had agreed to try Elamipretide. Therapy started immediately and we all hoped for the best. Days turned into weeks and weeks into months, and we watched our little boy grow stronger and stronger. Josiah is now at home and his heart function is stable. We are blessed that his doctors agreed to try Elamipretide as we know that Josiah's chance of survival was very slim. He is currently still on Elamipretide, and his doctors are in awe of the major improvement in his heart function.

I respectfully urge you to consider the urgency of this situation for families like mine. Without the approval of Elamipretide, we are left with limited options for managing Barth Syndrome. The approval of Elamipretide could offer a much-needed lifeline to children struggling with this debilitating condition, potentially transforming their lives, and giving them a brighter future.

Thank you for your time and consideration. I hope that, with your help, we can make a difference in the lives of children living with Barth Syndrome.



April Arguin
Community Member

Dear FDA Committee,

I am writing to you because the upcoming hearing for the Barth Syndrome community in regards to elamipretide is very important! I have received elamipretide for the last year and have seen incredible positive changes to my health. Thanks to elamipretide I am experiencing so many positive changes to my health. Since receiving the treatment, I have gained a tremendous improvement in my muscle weakness and overall physical and cognitive stamina. Prior to receiving the treatment, I was not able to stand up long enough to even make myself a simple meal, and relied on family members to cook so I could have a healthy meal. I was only able to walk about 5 minutes with the use of my walker, any longer I required my power wheelchair. I could only work on the computer 3 hours a day, and I needed to nap for an hour every afternoon. Now, I have been well enough to work 4-5 hours a day, I am easily making all my own meals again myself, I have had enough stamina to go to my local park several times for a picnic, I have gone out to dinner twice for the first time in five years, I was able to host a get-together at my house with my friends, I have now had three vacations this year, when I have previously not been well enough to travel at all for the past five or six years, and best of all, I have only needed my wheelchair once in the past 9 months!

There are literally not enough words to describe just how completely this medication has changed everything about my life, I think the best way I could summarize it all is that now with elamipretide in my life, I feel like I have gained back enough quality of life to want to continue living and that is everything. For people like us with serious, terminal, chronic illnesses, there will be constant pain, constant illness, constant challenges, constant suffering and our lives will look very different from our healthy, able-bodied peers. We know this, and we accept our fate in life, and we are not expecting or seeking medication to cure us, and make us as healthy as our peers, we understand the current scientific limitations. What we are seeking, is a medication to provide some level of relief, some level of easing our daily burdens, making it possible to do simple things like make a homecooked meal for ourself, to be able to drive a few minutes down the road to meet a friend for coffee, to be able to care for our cat, and to be able to spend more meaningful time with our families, and that is exactly what elamipretide has given to me, and is giving to so many others in these clinical trials, giving us a chance at a better quality of life.

Thank you listening to my words,

Sincerely,

April Arguin

Jamie Baffa

BSF Affiliated, Community Member

I can remember clearly the first time I learned my brother, Kevin, was sick. We were young, maybe five and six years old. Like many brothers at that age, we're playing hockey in the drive way. Kevin was the goalie, and I was trying to score on him. Eventually, I decided that it was my turn to play goalie. But before I could tell Kevin this was the case, our mom pulled me aside and asked if Kevin could keep playing goalie because he was tired, and when you're goalie you don't need to move around as much.

This happened before we knew what Barth syndrome was, but after far more hospital visits than any six-year-old should need to endure. And in the nearly 30 years since, they have only continued to mount. His fatigue has deepened – walking more than a block or two from the office where he works part time can wear him down to the point where it affects him more than a day after the fact. The common flu guarantees a hospital visit. He had to use a motorized scooter in high school because it was too difficult to get from one side of his high school to the other. Driving was never really in the cards, neither has moving out from our parents' house.

As proud as we are of the life Kevin has built for himself, we all believe he deserves so much more. He so values his independence, and we want him to have more. And a treatment that is both safe and effective, has the potential to give him just that. I cannot fathom how hard it has been for my brother to watch his siblings do things and reach milestones that he simply cannot. But elamipretide has the potential to change that. While it cannot give him the time back, it could give him more and, more importantly, allow that time to be richer, fuller, and easier than it has ever been.

Rosemary Baffa
Community Member

525,600 minutes x 35 years of being a mother, caregiver, and cheerleader to the most amazing, non-complainant, resilient, and indestructible of spirit young man, who happens to have Barth Syndrome.

His 1st heart failure at 10 weeks old at Johns Hopkins PICU with a diagnosis of Dilated Cardiomyopathy of an idiopathic nature. Prognosis…he will not survive.

From 3 months through 3 years, doctors talked of "failure to thrive" due to slower physical development. Surviving nonetheless with a sweet disposition and ready smile he could recite poems, sing songs and dance like no one was looking!

At age 4, another heart failure. It also quickly became clear that he was experiencing more than just heart issues. Muscle weakness led not only to physical and occupational therapy, but also to Ninja Turtle neon green leg braces from ankle to thigh. With his new look and a resolute, big smile, off he went to school with a hopeful determination to keep up with his peers.

Here comes 1st grade. Other boys are so much bigger in height and weight and show him who is the boss in very nasty ways. An incident of purposeful tripping led to stitches and for his teacher to prompt us to "send him to a new school". We did.

2nd to 4th grade. New school, no issues with being accepted. Thank God. Still delayed in growth, but academically stellar. However, writing and reading were tiresome. School was tiresome. Playing after school, tiresome. And then…

He suffered his first CARDIAC ARREST at age 11 weighing a mere 55 pounds. Fighting for his life and growth, he had a defibrillator installed and a feeding tube placed a year later. Cardiac arrests became more frequent, while middle school studies and socialization grew beyond challenging… but with the support of family and friends and the newly founded Barth Syndrome Foundation, he survived!

Armed with his ICD, feeding tube, and an IEP, off to high school went the smallest boy in the school. With the help of understanding teachers and administrators, "body guards" at school activities, and a motorized scooter, he got through the first two years without much medical intervention. However, a 6 inch growth spurt led to physical havoc with cardiac and muscle weakness, chronic neutropenia, and issues walking due to a weak ankle bone. A catheter ablation and an additional ICD lead interfered with much of junior year almost forced him to miss his Junior Prom.

While stability of arrythmias and heart function seemed to welcome the final year of high school, a major orthopedic surgery came shortly thereafter. Before we knew it, the decision to begin college became real and we simply had to figure out the logistics.

One class a semester, led to two classes a semester, then finally 3 classes a semester. Being dropped off and picked up at building entrances, elevators in said buildings, and a small campus worked well for his limitations. Persevering through several more cardiac arrests, he was able to not only keep up, but excel and graduate with high honors.

Now the real world. Cardiac issues, mobility issues, ineligibility for a driver's license, and endless medical appointments did not deter him from finding a worthy job turned successful career. Working part-time allows him to manage energy issues, and although heart failure and cardiac arrests continue to interrupt his work, they have not defined his spirit. Despite living with the trials of Barth Syndrome, our Kevin Baffa continues to be an example to all who know him of perseverance through adversity… with a smile!

Megan and John Branagh

Community Member

Dear Members of the FDA Advisory Committee,

We live in the San Francisco Bay Area with our 4 boys (ages 14, 12, 9, and 3). We are writing as parents of a child with an ultra-rare, life-threatening disease called Barth syndrome that currently has no treatment or cure.

Our 2nd son, Henry, is now 12 years old. He was deathly ill throughout infancy and as a young child due to severe heart failure. Thankfully, his heart is stable now (however Barth syndrome is extremely unpredictable, and our greatest fear is a fatal arrhythmia), but continues to take maximum therapeutic doses of serious heart medications, and will continue to do so his entire life. While these medications help his weakened and damaged heart to function, they do not address the underlying issue of why his heart is not healthy in the first place. Nor do these medications address the many other symptoms of Barth syndrome that strip life away from Henry every single day like the overwhelming fatigue, muscle weakness, and low white blood cells that make him susceptible to infection.

Barth syndrome affects every aspect of our family's life, every day – all of our daily decisions factor in Henry and his ability to access a full life, in more ways than we have to think about this with our other boys. From where we park the car to minimize walking, to where we go and what we do for family activities, to always knowing where the AED and the closest emergency room are. Our budget includes line items for Henry that are caused by Barth syndrome – medications, doctor visits, transportation costs, therapy. And the worry about his well-being and future are tenfold. Barth syndrome makes daily life for Henry extra difficult. For example, he wanted desperately to ride his bike to school, like other neighborhood kids, including his brother. But this is physically not possible for him on a regular bike. He wishes he had a fun elective like most of his peers. But he must use his elective period as a study class to keep up with his schoolwork, as a full day at school is exhausting not only physically, but mentally. He actually loves sports, and mentally has a desire and the coordination to play, but physically cannot keep up with his peers. This has forced him out of most organized sports at too young of an age. He gets frustrated at his inability to physically perform in the way he desires, and it is painful to watch. After a long and physically demanding day, Henry often ends the day by vomiting–one way in which his body says "enough".

This is all in addition to the emotional anxiety that he endures as he navigates living with an incurable and deadly disease that is not obvious to observers from the outside. He struggles with wanting to just fit in, yet wanting his peers to know why he can't. It is quite difficult to put into words what is at stake for Henry, our family, and the others affected by this devastating and debilitating disease. It is painful to know that a drug exists (elamipretide in our case), but that it may not ever be available. We respectfully urge the FDA to consider ALL data submitted in this final review of elamipretide, in hopes that the compelling positive evidence will lead to the approval of the first treatment for our ultra-rare disease. We are losing individuals much too young, and much too often – a treatment is necessary!

We remain hopeful that a treatment for Barth syndrome will be available in our Henry's lifetime. It is our greatest desire that he have a chance at a long and vibrant life, just like his brothers.
Sincerely, Megan and John Branagh

"The cruelest irony about Barth Syndrome is how deceptively healthy those who have it may appear. A casual observer would never appreciate them to have such a devastating illness." ~ Dr. Peter Barth

Our family has hosted an annual awareness and fundraising campaign benefitting the Barth Syndrome Foundation for the past 12 years, Happy Heart Week. We have hundreds of supporters, and have raised over $1M to date. To learn more about Henry's journey, our advocacy efforts, and our mission in ending the suffering caused by Barth syndrome, please visit our family's website, www.happyheartweek.com.


HENRY
(barth syndrome)
3 months old. Severe heart failure, unknown cause. 5 weeks in ICU. Referred to heart transplant team.
20 months old. Fed through NG tube for nearly 2 years. Globally develop-mentally delayed. Damaged heart from time in heart failure.
Thankful for a strong and able daddy who can help when walking is hard.
12th birthday. Grateful for life, even though it's more difficult than most.
Got an elctric bike that has allowed biking to school like neighbor-hood kids.
Our active, busy, crazy family, who desperately wants Henry to experience a long and vibrant life.

Alana Boozer
Community Member

I am writing to you to share my family's story and to plead with you to approve elamipretide as a treatment for Barth syndrome.

I grew up with two beautiful, younger brothers diagnosed with Barth syndrome, Evan and Michael. My brothers first became ill in January 1988, when Michael was admitted to the hospital with congestive heart failure. At one point, we thought we were going to lose him, and he was given his last rites in the hospital. He was only a year old. A week after Michael was admitted to the hospital, Evan was admitted with heart failure as well.

This was the start of a long journey looking for answers for Evan and Michael. Along the way there were lots of medications, doctors' visits, and hospitalizations. Between that first hospitalization and when Michael was five years old, my parents calculated that my brothers were hospitalized a total of 38 times. As a little girl in elementary school, I could often tell if one or both of them were hospitalized by the direction of my school bus route on the way home. If the bus went in one direction, I knew I was getting dropped off at the hospital to stay with the boys and my mom until my dad could pick me up when he got off work; if it was headed in another direction, I knew I was getting dropped off at my bus stop and that the boys were home.

My parents first learned of the nameless disease that would come to be known as Barth syndrome in June 1990, when Evan was in the hospital for the last time. Just a few short hours after reading the paper describing the disorder, Evan died. He was four years and eight months old. Following Evan's death, my mom did everything she could to find answers and to keep Michael alive. She eventually took him to Amsterdam to see Dr. Peter Barth and finally received confirmation that both he and Evan had Barth syndrome. She went on to find other individuals and families affected by Barth syndrome, and co-founded the Barth Syndrome Foundation. The passion, commitment, and dedication of all these families, doctors, and researchers involved with the Barth Syndrome Foundation have led us to this point today where they are asking for approval for the very first treatment of Barth syndrome.

Individuals living with Barth syndrome can be affected in different ways, but the one symptom that everyone experiences is debilitating fatigue. Michael often struggled to get through a full day of school because he was so exhausted. During his middle and high school years he was moved from in-person schooling to home and virtual schooling because he didn't have the energy. It took an emotional toll on him not being able to go to school with his peers or to share some of the same experiences with them. When we went on outings, we sometimes had to slow down or adjust because he would tire easily and struggled to keep up.

Michael died in December of 2009, just two days after his 23rd birthday and after waiting five months for a heart transplant that never came. There is not a day that goes by where I don't think about him or miss him. When he was alive, he would often participate in research for Barth syndrome and encourage others to do the same. He understood that he might not get to experience the benefits personally, but that because of his involvement in research, others would get that chance.

If he were alive today, he would be writing and speaking directly to you, advocating for this treatment to be approved, for this chance to improve his life and the lives of others. Elamipretide is a life-changing, life-giving treatment that has the potential to increase the quality of life for not only the person receiving the treatment, but their loved ones as well. It represents hope for this small but mighty community. My brothers didn't live long enough to see this moment but there are many others I care about who have. I don't want any other family to go through what mine has, or for anyone else to die waiting on a treatment. Too many have died already. I want everyone with Barth syndrome to have a chance to use this treatment and live their fullest lives possible.

Anonymous
Community Member

My husband and I have three children, two sons and a daughter. Both of our boys have an ultra rare disorder called Barth syndrome. It is a serious condition that affects many systems of the body due to the inborn error of metabolism. It causes every cell to be weaker, lacking energy. Our daughter may be a carrier of Barth syndrome but has not yet been tested.

From an outside perspective, looking at our sons one might think they look normal and healthy. It's difficult for some to understand what a devastating disorder Barth syndrome can be. Our sons can be treated as though nothing is wrong, but urgent medical attention has been required several times for serious complications.

We have spent weeks in the hospital due to heart failure, surgeries, and illnesses. We have had countless doctor appointments, lab work, testing, procedures, and advocacy efforts for our boys. Our sons are worth every effort, but it has taken its toll on us at times financially, emotionally, and mentally.

When both of our sons were in heart failure, it was obviously terrifying and stressful. We nearly lost our oldest son in infancy due to heart failure. Both boys take medications to make their hearts work better, but their heart muscles are not normal. Risks for serious and fatal arrhythmias are present.

One of the most challenging parts of Barth syndrome that affected us nearly every day was the area of eating and growing. Whether it be oral aversions, difficulty chewing and swallowing, fatigue, lack of desire, vomiting, weak muscles, or failure to thrive, we couldn't escape this burden most days. Our youngest son needed to have a G-tube placed as a toddler due to failure to thrive and still has it many years later. His tube feedings require a lot of time and attention to maintain.

Our boys have experienced several delays. They have received physical therapy, occupational therapy, and speech therapy. Our younger son has been especially delayed. He was finally able to walk independently just before he was four years old and required several aids to reach that goal with leg and foot braces, orthotics, and special therapies. One of his biggest struggles is his speech/language. He receives speech therapy three times each week. Having very delayed speech complicates many areas. It is difficult for our son to express his needs, be understood, make friendships, interact with peers and teachers, and learning.

Both of our sons require injections to strengthen their weakened immune systems. We must be cautious of illnesses and fevers. Infections can become life-threatening very quickly if their neutrophil counts are too low. Several emergency trips have been made to clinics and hospitals to treat illnesses. Over the years, many plans have been changed or canceled to avoid illnesses.

Worries of falling due to weakness and fatigue is often a concern. We have experienced multiple fractured bones due to simple falls. Often their arms and hands are unable to brace for impact due to a lack of rapid response time and muscle weakness.

The boys need a 504 plan and an IEP to ensure their safety at school and to help with their academic learning. There is a significant delay in learning and special education services are needed, including a one-on-one associate to help in all areas. Headaches and body aches are also regular symptoms for the boys. This affects learning, attentiveness, concentration, thinking, and conducting simple daily activities.

Currently, there is no cure or treatment for Barth syndrome, so having the possibility of Elamipretide as treatment for our boys is crucial for them. Getting Elamipretide approved could help in all these areas of concern and struggle for our boys. It would ease some of the burden on our family and improve our

quality of life. The benefits and safety of this drug, along with the positive impact it could have for our boys, our family, and the other individuals who are affected with this ultra rare disorder, is much needed.

Our boys' lives could depend on this treatment, so we greatly appreciate having this opportunity available.

"The cruelest irony about Barth syndrome is how deceptively healthy those who have it appear. A casual observer would never appreciate them to have such a devastating illness." ~ Peter Barth, MD, PhD

Sara (Sally) Burger
Community Member

Our son and grandson have Barth Syndrome. The disease is so rare that our son was not diagnosed until he was 19 yeas old even at a large metropolitan hospital having been followed his entire life by the then head of cardiology.

Life-threatening symptoms such as heart failure, cardiomyopathy, painful weak muscles, and chronic extreme fatigue limit their activities. Mild infections can easily become very serious. Extended hospital stays are the norm. Born 19 years apart, when they were toddlers the uncle and nephew took many medications and learned their colors from the medicines. Lasix- yellow, Carnitor- red, Digoxin-green and so forth. Depression and frustration from not being able to fully participate in life afflict them with diminished quality of life. Our son was so grouchy that his sisters nicknamed him Oscar the Grouch. The negative attitude was from being so tired and frustrated.

There is a positive part of this journey. For the past seven years our son, now in his mid 30s, has participated in a clinical trial to battle Barth syndrome. Elamipretide literally has transformed him into a new person. The doctors will present the clinical data, but I want to give my perspective as a mother and grandmother.

Elamipretide improved our son's heart function greatly boosting his energy level with increased strength and stamina. He was so weak as a baby that he did not walk until he was almost two. As he got older, he became cognizant of how much he was missing. He did not have the energy for extracurricular activities with friends. Sports were not a possibility with his weak muscles. Most activities had to be modified. He rode an electric bike. He was driven rather than walked at school and camp. As he got older, he did not want the modifications preferring to blend in with his peers. Realizing the modifications were necessary contributed to his depression. It was hard not having an active social life. As a teen he was fired from a ice cream shop job because he just could not scoop ice cream fast enough. We still do not eat that brand of ice cream.

With Elamipretide, the depression and anxiety are gone. He has friends and a social life. He goes out after work for dinner or to watch a ball game. He enjoys a 90 minute workout four times each week pain-free. At a wedding he actually asked his mother to dance! Imagine her delight! As a happy productive young man with purpose and direction he his advancing in his chosen field.

Oscar has left the building! He is living his life!

Following a successful heart transplant, our grandson still suffers the negative physical and psychological symptoms of Barth Syndrome. He wants so badly to do "normal" activities such as play baseball, basketball and ride a bike. In his teens, he simply does not have the vigor and strength. Like his uncle, our grandson is quite social and fun but invariably runs out of energy.

The disease affects all of the family members who sacrifice and modify their lives willingly and with grace. As an example, our daughter who is a Barth carrier and her husband chose adoption to grow their family.
The cruel fact is if the drug is not approved our grandson and other boys who suffer with Barth syndrome will not be able to fully experience life. Many boys whose disease is more severe will not live to begin Kindergarten. Without approval, our son faces losing access and reverting to his painful existence as before Elamipretide. That is inconceivable. It would crush his spirit along with the energy he depends on.

Similar to Cinderella at midnight, his world would disappear.

With first hand knowledge that the drug is effective and safe, I respectfully ask that you advance Elamipretide. This will give boys and young men the possibility for the opportunity to live the life that our son is gratefully experiencing.

Thank you.
Sara Walker Burger


GUEST 4 HOME
18 18
BALL STRIKE OUT
2

Darryl Byrd
Community Member

My name is Darryl Byrd, I am 42 years old, and I have Barth syndrome. I have known I was different for as long as I can recall. I was the smallest kid in my class in height and weight. I was bullied every day. I could not keep up with the other kids. I would get tired very fast and would need to sit down and rest. Most of the normal activities to my classmates were challenging to me. Running, climbing stairs to go to my next class, or even just walking took every bit of my energy I had.

Being out in the heat on a nice summer day was my Kryptonite and I was far from being superman. It's a feeling only a Barth kid could explain. Imagine having a certain amount of time to be outside before you began to melt? Memorizing my schoolwork was difficult. I always needed more time than others to complete my schoolwork. I had a lot of tutoring and after school help. I was put in learning disability classes because severe fatigue had an impact on my ability to pay attention.

I missed a lot of school due to hospital stays. For the first eight years of my life, I was hospitalized every 27 days. I was unable to carry a backpack to and from school. Even at a young age I suffered with severe leg and back pain.

I could not overexert myself without paying for it later. I had to learn how to manage my energy by only doing what was necessary. I suffered with depression and anxiety because I felt left out. I didn't fit in because of things I was unable to do. I was disqualified for jobs and friendships because of my disability.

I suffered from cardiomyopathy and cyclic neutropenia. Before a diagnosis no one knew why this was happening. Unlike my peers, I would land up in the hospital from a common cold or infection. I suffered painful mouth ulcers. Even a tiny cut, scrape or bruise could get infected without warning. I basically lived in Children's Hospital of Philadelphia on antibiotics and placed in isolation throughout my childhood and pre adult life. I felt like the boy in the bubble.

I was surrounded by Barth syndrome. My youngest brother Jamal, my nephew Jamil and my older brother passed away due to cardiomyopathy, which is fatal symptom of Barth syndrome. My nephew and my brother Jamal were weaker than me, so I was their caretaker. Not only was I living with Barth syndrome, watch people I loved die from it. Being their caretaker made me question my own health and daily aware of my own mortality. When a doctor told my brother he was he didn't have much time to live, I thought I was next.

Our symptoms varied; I suffered more from fatigue, muscle weakness and severe back and leg pain. They suffered more with cardiomyopathy and heart failure. I watched my brother die in horror.

I have two daughters who are carriers and a granddaughter who is possibly a carrier of this Barth syndrome. This breaks my heart. It will be tragic for me if I was to have to live through another generation of this horrible syndrome with my kids and watch my grandsons go through what I went through as a kid. Please consider approving elamipretide so that my family will have access to try this medication.

Linda Croxton
Community Member

The purpose for this communication is to make an appeal for approval of the medication Elamipretide HCl. It is very encouraging to consider the benefits this medication could bring to young boys with Barth syndrome to help them with their mitochondrial function. Healthy mitochondrial function plays such a critical role in the health and well-being of children with Barth. With the dysfunction that occurs, their energy process is seriously disrupted. This medication, with its mechanism of action which can reverse/attenuate mitochondral dysfunction, has so much promise for this population of boys/man. One of the really positive features is the favorable safety aspect of this medication.

This appeal is based on having had my life profoundly touched by two very special little boys who would be diagnosed with Barth syndrome. These were my two great nephews, Evan and Michael Bowen. At the time of their diagnosis, Evan was 27 months and Michael was 1 year old. They both experienced congestive heart failure at around the same time. They were two of the most precious and engaging little boys imaginable. They brought so much joy into our family. We felt so blessed to live in neighboring towns in the Tampa Bay area and getting to see them on a regular basis. It was so difficult seeing their health deteriorate, with the heart issues, neutropenia, muscular issues, failure to thrive and other issues. It was heartbreaking seeing them want to be able to do the things other little boys their age were going, but not be able to because of their heart dysfunction.

Our hearts were broken when we lost Evan at the age of 4 1/2 and then Michael at 23 years of age, waiting at Shands Hospital in Gainesville, FL for a heart transplant. Truly the loss of this little boy and later his now young adult brother left profound sadness in our lives. As it turns out, their mother would go on to make it her life calling to make a difference in the lives of other children here and around the world who were diagnosed with Barth syndrome.

Ladies and Gentlemen, I implore you to give a positive consideration to this medication as a potential treatment for Barth syndrome. It is so exciting to think how this could make a profound difference in the lives of these children and the families who love and care for them.

Thank you.



Anonymous
Community Member

September 26, 2024 Dear FDA AdComm Members, First and foremost, thank you for your participation in reviewing elamipretide as a potential therapy for Barth Syndrome.

Our son was diagnosed with dilated cardiomyopathy (DCM) just before he turned 3 months old. We spent 3 days in the PICU and thankfully he began to respond to the various medications. Fortunately, we had a very smart cardiologist who recommended that we conduct a genetic cardiac panel. While we thought having our tiny baby on cardiac medications was bad, the diagnosis of Barth Syndrome was devastating. So many and difficult aspects of the disease and no indication as to which and to what extent he would suffer from them. In the end, he has all aspects of the disease. I have highlighted some of the impacts that Barth Syndrome has had on our son and our family:

Heart: After his DCM diagnosis, our son immediately responded to the cardiac meds and his heart function improved. In hindsight, we probably made a major mistake by weaning him off meds completely. So, when the toddler growth spurt hit, we were chasing his declining function by weight adjusting meds and it got ahead of us. So, in the summer of 2020, not only were we panicked about the effects of Covid on our son and completely isolated, we were also dealing with a child in severe heart failure. At one point, we were probably one visit away from having to discuss a VAD/transplant path.

Neutropenia: Barth Syndrome has caused our son to have severe, chronic neutropenia. After countless ER visits where he was poked and screaming, we had to do something different. We elected for Neupogen injections which have been a game changer for us. Our son hates the injections to this day, but we have barely been to the ER since. But we were reminded just a few weeks ago how scary and fast moving a simple skin infection can be EVEN on Neupogen. We can never be too diligent.

Physical Strength and Endurance: After intense physical therapy, our son finally crawled at 11 months and walked at 20 months. However, he can by no means keep up with his peers. He is the smallest and slowest boy, often outperformed by the girls as well. He can barely ride a bike WITH training wheels. At almost 9, we already see him declining more with age, requiring him to take frequent rest breaks. He also struggles with keeping up at school, even with simple tasks such as handwriting.

Feeding: I would have never thought that feeding my child could be more challenging than managing DCM and neutropenia, but it TRULY is. To us, it's been consistently the worst part of the disease. We all have to eat 3 times per day and the constant nagging and begging him to eat is exhausting! But we learned the hard way about the potential for hypoglycemia. A few months into his diagnosis, he had been sick and not feeding well. Not realizing yet that it was one of the MANY aspects of the disease to be worried about, I rushed him to the ER with critically low blood sugar. I had no idea what was happening and thought he was dying of heart failure in my back seat. It was traumatizing! We were able to keep him off a feeding tube in the early years, but the transition to solids was full of gagging and vomiting. Not only was it messy, but it was socially isolating for our entire family. Unfortunately, we can't rule it out for his teenage years and beyond. We see him getting thinner and thinner by the day despite our best efforts.

The Scurvy "Incident": After our son was walking for a few months, we noticed that he would just fall down and whimper when standing. We took him to an orthopedist and he was diagnosed with a toddler fracture and casted. Six weeks later when they removed the cast and x-rayed, there was no evidence of healing. The doctor was puzzled and ordered an MRI, which we needed to have at the ER for expediency. Fortunately, there was a very astute ER physician who had one autistic patient with scurvy because he only ate oatmeal, and pondered whether it could be the same given our son's limited palate. It was confirmed. I called our pediatrician to tell him and his response was…"How did we miss that??" Even he was overwhelmed with the many aspects of Barth Syndrome that we were managing.

Financial: The financial implications of this disease on our family are great. We have hit our out-of pocket maximum of $10,000 every year since our son was born. Every year we budget for that in lieu of other options for

those funds. For the time being, we are able to do this but I am not certain this will always be the case. And this doesn't cover any of the external therapies, amino acid supplementation, and compounded enzyme blends that we cover personally. And we have no idea how much this costs our insurer annually. Siblings: Our daughter was only 2 when our son was diagnosed. She was often dragged to his appointments and now has severe medical anxiety as a result. As a preteen, we still deal with it and she often feels less important than her brother, even despite our best efforts to balance. It also turns out that I am a carrier of this horrible condition and had no idea. This means that my daughter has a 50% chance of also being a carrier. This is a fact that she is totally unaware of and one day we will have to discuss the topic with her.

Caregiver (Marital) Health: Having a medically complex child is extremely stressful and takes a toll on your mental and physical health. In those early years, we had MANY appointments (over 170 in one year alone) and both worked full-time. Somehow, we juggled with zero family nearby and managed to keep our jobs. Both of us also probably have unresolved PTSD from various issues over the years and managing his care has definitely taken a toll on our marriage at times. Additionally, since our son takes 4 cardiac medications, various blends of supplementation, and requires 3 injections per week, travel is more complicated for us as a couple and to see our family who live entirely out of state. Lastly, as a carrier, I carry tremendous guilt. Any time that he has a bad day/experience, I struggle all over again. Neither of my children know my carrier status and I dread the day that I have to share this. I am afraid they will hate me…what could be worse as a mother?

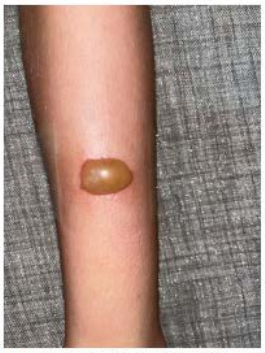
Thank you for reading this far. I had intended to keep this under one page, however, there is just too much to recount. We are extremely thankful that our son has lived almost nine years and much longer than we had initially expected. This is a truly a devastating disease for the patient and all who love them. My prayer is and has been that a treatment will be approved for ALL affected. Our son deserves to not only live, but to live a FULL and productive life.

Respectfully, A Barth Mom Committed to Saving Her Son

His size vs. his peers at almost 9 years old.
Some of these boys are younger than him as well.

Showing off his "muscles"…

Trying his best to jump with 2 feet out of the water.
He could barely get off the ground with both.



Huge blister on his leg from a bacterial skin infection earlier this September.

Wearing 4T clothes (which are big) at almost 7 years old.

BJ Develle
BSF Affiliated

My name is BJ Develle.

I'm writing to you as a close friend of this community who has been personally touched by Barth Syndrome.

Over the course of two decades, I have come to know a large number of the individuals diagnosed with Barth Syndrome and their families through my role as a volunteer, social worker, board member, and friend.

I have talked with caregivers about the realistic fears that their baby may not live long.

I have spoken with siblings who grew up necessarily hypervigilant to their needs of their sibling and struggled with the emotions associated with being a carrier of Barth syndrome.

I have sat with individuals diagnosed with Barth syndrome and processed feelings of anger, frustration, and desperation over the life that they have missed out on, or may never achieve.

I have listened to the statements about how, other than providing material for testing to benefit the younger patients, life has lost its meaning because of the limitations that Barth syndrome brings.

I have sat in the hospital with my close friend waiting for a heart transplant, us both knowing he likely wouldn't live long enough to see it save his life.

I have grieved alongside the community as we say goodbye to another person who died before an effective treatment could be found.

I have said goodbye to far too many young people… too many friends. (Three of the 4 in the attached photo are deceased)

And for once this community, specifically those diagnosed with Barth syndrome, have hope in Elamipretide. Some have felt what it feels like to live a life filled with quality, and not fear. One young many once said that after being on the medication, he knew what it was like to not be sick, for once in his life. If he had to go back off the medication, he said he would rather be dead.

Please approve Elamipretide so that others may have the opportunity to experience an increased quality of life and hope.

Sincerely,

BJ Develle

Kevin Dollard
Community Member

My Barth syndrome story started on June 30th, 2008, when my son was born. This day is permanently carved into my memory for life. What should have been a joy and a new beginning, became a day engulfed with fear and sadness. When the Doctor gave us the news of our son's condition, I compared it to the stories people tell of near-death experiences. I felt out of body, I was above myself; the voices were as if I had my hands over my ears, it turned dark instantly in the room, this must be a dream, this can't be real. The doctor told us our son was in severe heart failure and was being sent to the intensive care unit. The news was not good, and prognosis was worse. To be told you should spend as much time the next few days with your newborn son was devastating. I spent the next two weeks praying sleeplessly, praying angrily, praying this was a dream, begging to have the infliction and this burden be given to me so this child would survive. Henry was allowed to come home, I knew what I was being told without a word, he was being sent home to pass. This was the start of our Barth Syndrome journey, but not the end.

The diagnosis was initially heart failure, after 18 months in and out of hospitals Henry became extremely ill, he spent the next two weeks in ICU with a bacterial infection, this is when we found out he had Barth Syndrome. Henry's Barth Cocktail is dilatated cardiomyopathy, chronic neutropenia with white blood counts of O and mitochondrial disease. We felt defeated, as if the deck was being stacked against Henrys survival. We found hope in a seemingly hopeless situation, when we were approached by a mother, named Shelley Bowen. At that time, she had pulled together a group of parents from across the globe who had boys inflected with this ultra rare disease. We began to learn how to try and manage our sons' medical dynamics

Describing what it's like to be a care giver and/or describing how your son feels is extremely emotional and complicated. It's a daily acknowledgement of mortality and a low-quality standard of life. Over the last 16 years, I have often been asked the same questions; What is it like to have a medically fragile child? How do you manage? Is it emotionally draining? I can't say I ever have eloquent answers, something enlightening for those who ask; I mostly avoided answering the question because I felt most could not manage the emotional burden of truly understanding what Barth Syndrome was and what it is like to live with this diagnosis on a daily basis or more importantly what Henry has to deal, physically, emotionally, and mentally. I have chosen to use single words or analogies in trying to explain and only elaborate for those strong enough. These words are uncertainty, pain, despair, fear, hopelessness, anger, and cursed. Analogies or stories: Everyday felt grey and gloomy for years like a perpetual depressing fall day. Imagine sharing your bed every night for twelve years with your son out of fear he would die during the night, and you wouldn't be there to help. Realizing your 12-year-old son now wants to sleep in his own bed and you need to let him do this, because it is time. However, you spend the next 4 years waking up in the middle of the night to make sure he's breathing.

What we are asking for is hope. In a world where there are limited treatment options for ultra rare diseases, to those affected. Energy to enjoy their days to the fullest. We need hope for the sons that have survived and have an opportunity to live, hope to improve their quality of life, hope to have some resemblances of normality. Elamipretide offers hope a in generation of hopelessness, for the sons and parents to have a viable therapeutic option for treating some of the symptoms that Barth Syndrome limits our sons daily. Our small group is begging you to provide this hope for our rare, young, affected boys and men.

Bryan Drake
Community Member

To the FDA Advisory Committee,
I am writing to you today to shed light on the daily struggles faced by my 17-year-old son, Abram (he likes to be called Abe), who is living with Barth Syndrome. I believe Abe would greatly benefit from the FDA's approval of Elamipretide.

Abe's life has been challenging from the start. Diagnosed with failure to thrive at 3 months of age, he lacked the muscle strength to breastfeed or even bottle-feed effectively. He wasn't getting the nutrients his body desperately needed. At 3 months old, we spent two agonizing weeks in the hospital trying to uncover the cause of his poor health. The hospital staff even accused us of child abuse, forcing us to interact with Child Protective Services.

After determining we weren't harming our firstborn child, Abe endured a battery of tests. He saw more needles in those two weeks than I've seen in my entire 31 years! Test results trickled in one by one: an enlarged heart, severe neutropenia, but no 3-methylglutaconic aciduria. Initially, Barth Syndrome was ruled out. My wife (now ex-wife, due to the strain of raising a special needs child) and I knew it was Barth Syndrome because of her family history, but we had to convince the geneticist to run the test. A full year later, we finally confirmed Abe had Barth Syndrome.

Abe's childhood was far from typical. He missed developmental milestones, taking 3.5 years before he could even stand on his own. Even then, he could only manage a few steps before fatigue set in. His low muscle tone and cardiac insufficiency made it impossible to keep up with his peers at school. He struggled to make friends, always standing out as the boy who rode a scooter and needed help carrying his books. Due to spending so much time with adults in hospitals and clinics, Abe lacks social skills. He frequently misses school for appointments, fatigue, or Barth Syndrome-related issues like nausea and diarrhea. His IEP is 8 pages long – no single teacher can possibly address all of Abe's needs in a classroom setting.

Abe has an implanted cardiac loop recorder due to his enlarged heart and the risk of sudden cardiac arrest. We constantly monitor for irregular rhythms. Wherever Abe goes, his Automated External Defibrillator goes too. Thankfully, he hasn't needed it yet, but we know other boys who've required AED or ICD shocks – a traumatic experience for all involved.

Abe's condition limits his activities. Heat, walking distances, or prior exertion can easily wipe him out. He has a scooter, but using it in high school draws unwanted attention. He longs for a girlfriend like his friends, but Barth Syndrome makes him look and act differently. He's even afraid to start driving, fearing even a minor accident could be fatal. Fatigue from turning the steering wheel is another concern, highlighting his future need for transportation assistance.

Finding full-time employment after graduation will be yet another hurdle. His IEP allows for a shortened school day, but the real world won't offer such accommodations.

At 17, Abe is increasingly aware of his mortality. He knows he could die suddenly from cardiac arrest or an infection his weakened immune system can't fight. He battles depression but strives to remain positive. We pray daily that Elamipretide will be approved. It offers hope not only for Abe but for all the boys we've met who share similar struggles. They deserve at least one proven therapy that can improve their lives.

Thank you for your time and consideration.
Sincerely, Bryan Drake

Laura Drake
Community Member

September 26, 2024
To whom this may concern:

My name is Laura Drake, and I have a nephew, Abram Drake, that is living with Barth Syndrome. I'm writing in support of approval by the FDA of the drug Elamipretide.
Looking at Abram you wouldn't ever think that he had a rare and life-threatening disease called Barth Syndrome. He is a happy kid that is just trying to be "normal" and fit in with other kids his age. I want that for him, but things haven't been that easy for him due to the fatigue that he lives with.

From birth there were clues that something was wrong. I remember issues he had with feeding. He had to be on a feeding tube for much of his first year of life due to swallowing difficulties and an enlarged heart. He has had issues with speech due to muscle fatigue and weakness. He didn't have the energy to run and play with his cousin, my daughter, when they were younger.

As he has gotten older he hasn't been able to do some of the basic things that we all take for granted such as walking to classes. My nephew uses a motorized scooter to get a round at school. These challenges are just a few of the many that he faces daily.

Abram is 17 years old now and realizes some of his limitations and is trying to cope with them the best he can, but the approval of this drug could help him have a much better quality of life and live more "normally".

Thank you for your thoughtful consideration of this drug.
Sincerely,
Laura Drake
10242 Foster St.
Overland Park, KS 66212

Sarah Drake
Community Member

To the FDA Advisory Committee,

I am writing to you today to shed light on the daily struggles faced by my 17-year-old stepson, Abram (he prefers to be called Abe), who is living with Barth Syndrome. I believe Abe would greatly benefit from the FDA's approval of Elamipretide. This drug offers real hope for improving his quality of life.

I came into Abe's life when he was about 3 years old. At that time, we were limited or unable to do a lot of activities with Abe that other kids his age were doing because of his fatigue and concerns with getting sick. These were things that all families do like go to a pumpkin patch, play games outside, walk the dogs, or trick or treat. Even a short walk in the park would leave him exhausted. Travel plans were also limited as we had to think about the risk and access to medical treatment. Therefore, Abe has missed out on all those lasting memories of family trips and seeing new places.

As a result of spending so much time with adults in hospitals and clinics, Abe lacks social skills. It is harder for him to develop connections with others and lasting relationships as he is often limited in what he can do, and this can be very isolating. The pandemic also made this so much worse for him. Because of limited activity and isolation, his mental health has been impacted. He lacks confidence in himself and questions what he has to offer other people.

Looking ahead, Abe is 17 and has started to think about his future. This is a time that should be exciting for him, but it brings so much uncertainty and doubt for him, and that is heartbreaking. With everything he has gone through, he hasn't really had the opportunity to gain independence, and so for him the thought of the next step is overwhelming. It's hard to think about who you want to be and what you want to do when you have grown up knowing that your time is limited because there is no cure for your genetic condition. He will likely need to be on government assistance and other programs to help him become independent, and he will struggle to be self-sufficient.

We hope that Elamipretide will be approved. It offers hope, which is something that Abe would benefit greatly from. Abe deserves a chance to have more, and so do all the others who live with Barth Syndrome.

Thank you for your time and consideration.

Sincerely,
Sarah Drake

Mike Dubuque
Community Member

My name is Michael V. Dubuque, I live in Hamilton Township, Mercer County, New Jersey. I'm writing this on behalf of my nephew, Declan Comerford.

At 11 months old, while on Christmas vacation to New Jersey with his Mother Jamie and without warning, Declan suffered full cardiac arrest. After twenty minutes of intense work to revive him, a medi-vac flight from Ocean Medical Center in Brick over to Jersey Shore Medical in Asbury, he was transferred by ambulance to the Children's Hospital of Philadelphia. Critical, but stable and on life support, weeks into this nightmare with no answers as to what exactly happened, a genetic test came back with an unfortunate reality. Declan had been diagnosed with the ultra-rare condition: Barth Syndrome. Open heart surgery and the installation of a Left Ventricular Assist Device (LVAD), the promised need for an eventual heart transplant were the only future the Doctors saw for my nephew. Thanks to Johns Hopkins, along came an experimental miracle drug under the expanded access program, named Elamipretide. This therapy has afforded Declan a life where he is living freely and absolutely thriving. Declan is the only known child to be taken off of a VAD, as well as the transplant list. Cardiologists who have reviewed his case, say they would never know he even suffered such a trauma without seeing his medical history. His native heart beats strong. Thank you Elamipretide.

As a proud representative for my nephew and his tiny community of Barth Brothers, along with the Parents, Aunts and Uncles of those living and especially those lost to this ultra rare disease, I say thank you, to the FDA for hearing our voices. We appreciate the decision to fairly review Elamipretide and upon full approval of its use, give these Barth Boys and Men a fair shake at a long and fruitful life.
Everyone deserves a chance to actually live. I remain hopeful the FDA understands this and will see that Elamipretide provides us with this opportunity.

Amy Enroughty
Community Member

Amy Enroughty
1812 Bellows Drive
North Chesterfield, VA 23225
amyenroughty@gmail.com
(804)514-1769
September 23, 2024

FDA Advisory Committee
Food and Drug Administration
10903 New Hampshire Ave
Silver Spring, MD 20993

Dear Members of the FDA Advisory Committee,

I am writing to you today as the mother and primary caregiver of my 10 month old son, Owen, who lives with Barth Syndrome, a rare and devastatingly life-altering condition. I plead with you to ensure the fair, equitable, and timely review of Elamipretide for the treatment of Barth Syndrome, as it offers the possibility of hope and a better future for children like Owen.

Owen's diagnosis has placed an unimaginable strain on our family. His condition, which includes neutropenia, significantly increases his risk of infection and severely limits his ability to interact with the world. While other children his age, including his sister, are able to attend daycare and enjoy the social experiences that come with it, Owen is isolated. This isolation has limited his opportunities to grow, learn, and connect. I have seen firsthand the profound impact this has had on his development, and it breaks my heart every day to see him miss out on experiences that his peers take for granted.

Owen's Barth Syndrome diagnosis has profoundly disrupted our family's daily routine and drastically altered our lives. Due to Owen's compromised immune system, frequent medical appointments and the intensive care he requires, I went from being a working mother to a full-time caregiver, a role that is both rewarding and overwhelming. The financial impact has been devastating. We've lost over 50% of our household income, and the cost of Owen's medical care only adds to this burden. Beyond the financial strain, the emotional toll is significant. I've had to forgo the social connections and independence that working provided, leaving me isolated and under immense psychological stress.

Our lives have been reshaped by this disorder in ways we never could have imagined.The psychological and emotional toll is immense, as we try to navigate the challenges of raising a child with such a rare and serious condition, all while facing the uncertainty of his future.The lack of available treatments for Barth Syndrome leaves us feeling hopeless at times. It is like setting out on the journey of parenthood, only to discover that the boat you are in has sprung a leak—and there is no way to patch it. You have all the tools you thought you needed, but none are enough to address the crisis at hand. The entire family is affected, and there is little relief in sight.

Elamipretide represents a potential lifeline—not just for Owen, but for all families affected by Barth Syndrome. Those who have been granted access to this drug have experienced life-changing improvements, and it offers a glimmer of hope to families like ours. The possibility of an approved treatment is not just about managing symptoms—it's about restoring some semblance of normalcy, easing the enormous burden on caregivers, and giving these children a chance at a fuller life.

There is a quote on the wall where I take Owen for treatment: “Every child is born with great potential. Shouldn’t every child have the chance to achieve it?” I urge you to consider the authorization of Elamipretide with the utmost care and empathy, knowing that for us, and for many others affected by Barth Syndrome, this decision is not just about medicine. It is about offering hope, a future, and the chance for a fuller life to those living with this ultra-rare condition, as well as to the families who love and care for them.

Sincerely,
Amy Enroughty

Luke Farris
Community Member

My name is Luke and I suffer from an ultra-rare disease called Barth Syndrome. I am 18 years old, but I feel like I'm 100 years old most days.

For me the biggest thing Barth Syndrome does is it affects my daily life by causing me to have a lack of stamina such that I feel overwhelming fatigue. I have so little stamina that I can barely walk some days. On a well rested day, I can walk leisurely for about a quarter mile before I have to take a break. During the school day I'm exhausted both mentally and physically, but I know I just have to make it through until I get home so I can take a nap. If I push myself too far, I spend the whole next day in bed trying to recover from the exhaustion. When I reach my point of exhaustion, I feel like I am about to crash. When I'm at that point my legs start to wobble, my knees get weak, my feet start hurting, my breathing gets labored to where I can't catch my breath, I get light-headed, and I develop a rapid heart rate.

Over the years I feel like my condition has worsened. I feel like when I was younger, I definitely had more energy and was capable of more physical activity. Even though I had more energy back then, I still couldn't really keep up with my peers. I would get winded and feel weak just from running around the playground for a few minutes. Nowadays I feel like I need to take more frequent breaks even with simple things like walking from classroom to classroom during the school day.

Now that I'm older I've gained weight because I don't have enough energy to exercise. I feel like my condition has also hindered me from making long term friendships because I'm so exhausted after school, I can't go hang out with classmates to forge those lasting bonds that I would like to form. After my diagnosis at 14 years old, my parents have looked back at my childhood and realized that all my issues were caused by Barth Syndrome.

From not latching on during breastfeeding, to only being able to take about half an ounce of formula at a time, to having to take physical therapy to learn how to walk, to not being able to play sports due to my muscular fatigue, to being sicker than anyone else in my family, to having mouth ulcers all the time, to having a rapid heart rate, to having a difficult time with math, to having ADHD, to having depression, to having neutropenia—It all leads back to Barth Syndrome.

Meeting with my Barth family this past July at our biennial conference and seeing some of the older affected men, it scares me to think about my future. A lot of them have to use mobility scooters just to get around at 30 years old and up. I implore you to please help me and others like me who suffer from Barth Syndrome have hope of a more fulfilling and longer life by supporting the approval of Elamipretide as a treatment for Barth Syndrome.

Thank you!
Luke, Barth Syndrome patient

Kellye Farris
Community Member

My name is Kellye and my 18-year-old son, Luke, has an ultra-rare disease named Barth Syndrome. Luke was diagnosed in 2020 at 14 years old after 2 and a half years of extensive genetic research to figure out why he had Neutropenia. All the signs of Barth Syndrome were there as Luke grew up, but this rare disease was not on our radar.

As an infant Luke was unable to latch on to breastfeed even after six months of trying; and he could only take in half an ounce of formula each time he took a bottle. As a toddler (18 months old) he had to have Physical Therapy to learn to walk. At the time we didn't know he had a condition that caused this issue due to the muscle weakness and fatigue of Barth.

As a child he was not able to keep up with his peers. I recall one time his Bible study teacher commenting that Luke gets so winded and fatigued just when playing on the playground for a few minutes as a 6-year-old. He attempted two different times during his childhood to play soccer. Both times he had to drop out because he just could not physically run up and down the field without feeling like he could pass out and his legs feeling like jelly. As a child/teenager he was always the one in our family who got sick. We could not figure out why he would come down with a fever so often. Later we discovered this was due to Barth Syndrome related Neutropenia.

As a teen we went to visit a cave one time, and Luke had to stop and rest every few minutes because he would get so fatigued and feel like he couldn't breathe. He recently turned 18 years old and he said he feels like an old man because he doesn't have the stamina to do much of anything but sit around. He's a senior in high school and usually comes home each day to take a nap because school physically and mentally wears him out. This not only impacts his schoolwork but also his relationships with his peers.

Although Luke seems healthy on the outside, that can change very quickly. We have to be aware of any fever, infection, or heart issue because he will need to be seen by a doctor immediately in order to intervene as soon as possible. We've learned a lot about Barth Syndrome and the many severe symptoms that affect Luke's heart function, muscle tone, energy, feeding, mobility, and learning. It pains us to see the older guys with Barth Syndrome struggle to enjoy life with very little energy. People with Barth have a shorter lifespan. We are terrified when we think about the future for our son, and how there is no current approved treatment to help him. It feels hopeless to be part of such a small group and makes me feel like nothing will ever be done to help the Barth community. The debilitating fatigue leads to depression in a large portion of those afflicted with Barth including Luke, who takes medication to help with this.

I don't want my son to have the energy of a 100-year-old when he's just starting his adulthood. I have seen the results of the studies with Elamipretide, and desperately hope that we will soon be able to try this drug for our son. Currently he has nothing available. Please consider being as flexible as possible in your review of Elamipretide to give Luke hope for his future.
Thank you, Kellye

Phil Farris
Community Member

My name is Phillip and I am advocating for my son, Luke, who suffers from Barth syndrome. As an infant Luke could not metabolize all the nutrients in his baby formula and would promptly vomit several times during feedings. His stomach was empty and he was hungry, but his body just couldn't process all the calories, causing trips to the Emergency Room to have feeding tubes placed. At one visit, the ER doctor told us that Luke had "given up." My stomach churned at this news and I decided that I would have to fight for his life on his behalf. His development was delayed to the point that I carried him everywhere if he wasn't in the stroller. It wasn't difficult for me because he was so small, which is a side effect of having Barth.

At every visit to the pediatrician, we were shown Luke's slow gains on the growth chart with his growth mapped alongside the standard. We were told that he was just growing at his own pace. When Luke turned 8 years old, he joined the Cub Scouts and we went to camp. With there being a chapel service on the first night, we were all hiking up to the top of a hill to reach the outdoor chapel. Luke cried all the way to the chapel, saying, "I'm too tired!", as tears streamed down his face. At the time, we had no diagnosis and so I was insisting that he make the trip. Luke was diagnosed with Barth Syndrome at age 14. I now know that he was exhausted from the disease that none of us knew he had. His fatigue has continued into his teens and is something that will always be a problem for him.

Since his diagnosis, Luke has been admitted to the hospital about a dozen times for various infections or fevers. Because neutropenia is a part of Barth syndrome, any abrasion to the skin brings the risk of infection and those infections are treated with IV antibiotics as an in-patient.
As a high-schooler, he regularly comes home from school and immediately goes to bed to recover from the day. Physical exhaustion is a daily battle for Luke. Barth syndrome patients' life expectancy is about 45 years. Luke, being 18, is facing his own mortality in the fairly short-term.

It is my request that Elamipretide be approved for use by Barth syndrome patients. Luke's quality of life and even his life expectancy could be greatly improved by this drug.
Thank you for your consideration, Phillip

Filchak Family
Community Member

Greetings FDA Review Committee, My name is Caroline Filchak and I am the proud mother, of a 3-year-old little girl, with Microthalmia with Linear Skin Defects syndrome (hereinafter "MLS syndrome"). MLS syndrome is a mitochondrial disorder and her syndrome has caused her to be born with deafness, blindness, agenesis of corpus callosum, Wolff-ParkinsonWhite syndrome, and cardiomyopathy. We named our miracle daughter, Hope, and her name serves as a reminder, to us, that we serve a God who is faithful and who we put our hope in, even in hard and uncertain times.

Soon after Hope was born, we were recommended by our local team of doctors, here in Georgia, that we should visit the Children's Hospital of Philadelphia (CHOP), to learn more about our daughters' mitochondrial disorder. Over the last three years of Hope's life, we have visited with CHOP several times and we have received nothing but outstanding care. During one of our routine visits at CHOP, Hope's doctor mentioned, that if her heart function ever started to decline drastically, there was a clinical trial drug, elamipretide, that we could administer to Hope that was having a very positive impact on children with similar heart conditions.

Hope was born with 2 heart conditions - Wolff-Parkinson- White syndrome and cardiomyopathy. Until last year, we have been able to manage them through oral medication, diet, and rest. Throughout Hope's short three-year life, her ejection fraction has always measured between 56%-60%. Sadly, in January of this year, her ejection fraction dropped from 60% to 46%. It seemed as if her cardiomyopathy was progressing at a drastic rate and her heart function was declining rapidly. It was the first time, in her life, that we had seen such a drastic drop in function and as any parents would react – we panicked and were in search for anything short of a miracle to help our little girl's heart and to basically – save her life. We quickly remembered the trial drug, elamipretide, that her doctors had mentioned early on in her life. Without any hesitation, we immediately called her team at CHOP and they approved Hope to start, elamipretide, in February of 2024.

We have seen a radical improvement in how Hope feels and functions, since she began taking elamipretide. At the end of last year and January of this year, when her heart was not functioning at normal levels, she would sleep daily, ranging anywhere from 11AM to 2PM. There were many days that she slept until 2PM, only to be awake for 6 hours, before going back to sleep at 8PM, for the night. She missed a lot of school because she slept so much and her speech regressed because she was only hearing sound for 6-8 hours a day. When she was able to go to school, she would often times fall asleep at lunch or during other activities, and she was never able to fully enjoy a typical day at school like her peers. We also had to cancel a lot of her early intervention therapies – which are of the upmost importance for her development and progression on her oral, gross motor, and fine motor skills. If able, we would move them to the afternoon when she was awake – but this varied daily and was difficult to arrange last minute.

Hope has experienced and we have witnessed many positive and encouraging effects, since she began taking elamipretide. We have seen her heart function maintain at an ejection fraction of 46% - which is excellent! We have seen her BNP level decrease from 92 to 70.1 and we have seen her regain the energy of a typical 3-yearold. Hope started back at school, in August, and she has made it to school, on time, every morning. She is no longer falling asleep during lunch or other activities but instead, she is participating in music class, playing with her friends, and learning her ABCs. She is living and thriving because of elamipretide! Her favorite activity at school is to play in the indoor gym; before elamipretide, this wasn't something that she was able to experience, while she was at school. We finally feel like we have had the opportunity to see Hope fully enjoy life, since starting elamipretide. We are so grateful, for the opportunity, that she has been able to take this miracle drug – it has truly changed her little life!

We know the group of families and kids that this drug impacts is small but they are surely mighty and don't lack perseverance; most of these families and kids, that are impacted positively by elamipretide, have such a rare syndrome, there is not going to be a large percentage affected. However, this drug has had a drastic impact on how Hope feels and functions and event where it saves kids' lives. We have seen the positive impact elamipretide it has had on her heart and energy levels and are hopeful that it will contribute to a long-term survival for our child living with cardiomyopathy and a mitochondrial disorder. I beg you, on behalf of my child and others like her, please approve this drug and give these children the opportunity they deserve to live a long life.

Thank you so much for your consideration and for taking the time to read our letter.
Thank you, Ben and Caroline Filchak Carobower10@gmail.com 678-617-9654

Johan Fioole
Community Member

Letter to the FDA Advisory Committee
A Life with Barth Syndrome
As an older patient living with Barth syndrome, I want to share my journey with you. It started right after I was born. Within three months, I was admitted to the hospital and stayed there for nine months. At that time, no one had heard of Barth syndrome.

Growing up my life was different. During school, I didn't participate in physical activities such as gym, swimming or straining school trips, because I couldn't. I also stayed away from the "wild" games other children played during recess.

As I got older, my oldest sister lost her first son. He was weak and had heart issues, but at that time, we had no idea about Barth syndrome. Fifteen years later, she lost her second son, who had the same symptoms. By then, we had heard of Barth syndrome. He was tested, and they found the genetic marker for Barth syndrome in his DNA. The disease and death of both boys had an immense impact on our family.

In the years that followed, I met my wife and had children. Although I had to live at a slower pace, life felt relatively normal. But after our first daughter was born, life became more intense and exhausting. Sleepless nights, coupled with the physical demands of caring for a newborn, took their toll on me.During that time, my heart issues worsened. Because of my family history, they tested me, and I was diagnosed with Barth syndrome.

Now, I'm treated for cardiomyopathy and monitored for muscle weakness. I follow strict guidelines for food and physical activities, as much as my body allows. I always plan activities as much as possible in the morning. Because then I have some energy. In the afternoon I always sleep for two hours. Otherwise I do not manage it through the rest of the day, Evening activities are out of the question because of the fatigue. Unfortunately, I am no longer able to work due to chronic fatigue. As I get older, my activity level decreases, and for several months now, I've had to rely on a mobility scooter. For the near future my doctors and I expect that I will need a stair lift and a walker to be able to walk small distances.
One of the things I hope that I will not have to go through again is surgery (Placing crt-d with leads) while I am awake with only local sedation. This was because of the risk of total anesthetics of a Barth patient.

Looking ahead, my biggest concern is for my daughters and their future children. Both of my daughters are carriers of Barth syndrome, and I know there's a significant risk that my grandsons could also have the condition.
Thankfully, we now know much more about Barth syndrome and have made strides in treating its symptoms. But the next crucial step is finding a medication that can improve the physical health of Barth patients.

Elamipretide has the potential to be the first medication that could achieve this – if approved by the FDA. On behalf of my family – my wife, daughters and not-yet-born grandchildren, I urge this advisory committee to support approval of Elamipretide. A positive decision would provide much-needed hope to the Barth community and move us forward in finding effective treatment options.
Thank you for your consideration.

Michelle Florez
Community Member

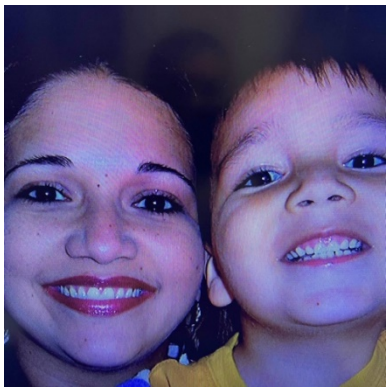
My name is Michelle Florez and my oldest son, Michael Anthony Telles Jr. suffered from Barth Syndrome. We received his diagnosis when he was a year and a half old during a 3 week stay in the ICU due to heart failure & sever neutropenia. Michael died when he was seven years old on April 20th, 2009, due to Barth Syndrome.

Michael suffered from sever muscle weakness, neutropenia, growth retardation, and diminished heart function. When he died at the age of seven and was in the 1st grade, he only weighed 40 pounds. There were no treatment options. The best we could do was manage his symptoms with heart medications and neupogen. There was no treatment for his weak muscle or his low energy levels. He would become worn out from normal activities and his poor function and would then have to sleep for several hours to recover. He couldn't run in P.E. class, he couldn't go out and ride a bike, and he couldn't play sports because it would wear him out. He was also sensitive to the heat and living in Texas that meant he had to be inside for more than half the year.

Mentally this took a toll on Michael and me because I had to watch my child sit on the sidelines and not be able to participate with the other kids when they were out running around. It broke my heart. Living without my son every day is a pain and a loss I cannot full articulate, and I miss him every day and would give anything to have him back.

These people affected by Barth Syndrome deserve hope, they deserve some semblance of a normal life, they deserve some type of treatment! They deserve to have energy to run with their friends. A chance to feel better & not suffer from so much pain.

If I had the chance to give my son this treatment, I would take it in a heartbeat! Please give them this chance!!



Kevin Freiert
BSF Affiliated

Kevin Freiert
CEO, Salem Oaks Consulting
VP and Board Member, Rare New England 216 Beckwith Hill Drive
Salem, CT 06420

October 1, 2024
Submitted to docket FDA-2024-N-3969 Dear FDA Reviewers,
I am writing to personally request a fair and appropriate review of the data in the New Drug Application 215244 for Elamipretide Hydrochloride Injection.

I have 37 years of experience in drug discovery and development, including well over a decade in rare diseases. I also have worked closely with the Barth Syndrome Foundation over the past few years to help them tell their stories and prepare for this moment; the moment when hope meets judgment.

During the upcoming Advisory Committee, you have asked a number of experts to provide their learned opinions about the strength of the data and of the evidence of efficacy and safety for elamipretide. I submit that the real experts in this specific condition are going to speak during the Public Comment period. They too will be presenting evidence that you must consider. In fact, they have spent more time with Barth syndrome than any clinical trialist or treating physician could ever accumulate. Yes, they want a treatment but that does not disqualify their observations.

A key part of your decision and your judgment will be benefit:risk. Given the rarity of Barth syndrome, it is very difficult to apply conventional wisdom to the data collected. The sample size in the pivotal study is very small. You may rightfully ask how you can grant approval based on the data from just 12 boys. But the TAZPOWER trial is not the only evidence you have in front of you.

Even with the small sample size, the data from the trial are very strong. Statistical significance was achieved at 36 weeks in improved measures for:

- 6-minute walk test (m), (95.9 m improvement from baseline)
- Barth Syndrome Symptom Assessment (BTHS-SA) total fatigue scale (mean score.) One of the most important factors affecting the quality of life for these boys is fatigue, crushing fatigue,
- Patient Global Impression (PGI) of symptoms (mean score),
- Muscle strength measured by handheld dynamometry (HHD) (newtons),
- and the EQ-5D questionnaire.

Normally, a sponsor would increase sample size to reach the level of statistical significance. Since significance was already reached, the concern about a small sample size for these efficacy measures is moot.

The other efficacy measures while not achieving statistical significance consistently showed a favorable effect at 36 weeks:

- Promis Fatigue [mean score],
- Clinician Global Impression [CGI] of Barth syndrome symptoms [mean score],
- and SWAY balance

In addition, left ventricular stroke volume increased significantly in these trial participants. This is an objective measure that is indicative of improved cardiac health.

But you may question the 36-week data since the trial was designed to look at 12-week data and those data failed to reach statistical significance. You have surely seen similar situations with other rare diseases. With approximately 300 boys with Barth syndrome worldwide, the knowledge about disease progression is thin. It should not be surprising that a sponsor made some errant assumptions in the original clinical trial design. In this case, the treatment and observation period required to see separation between groups was too short.

And there is more evidence that demonstrates efficacy.

- Natural history data, with matched pairs, shows that elamipretide provides benefit
- Anecdotal data, including a toddler being removed from LVAD, demonstrates how consequential that benefit can be.
- Accounts from those discontinuing the studies indicate that their condition reverted and worsened when elamipretide treatments were stopped.

Which brings us to risk. The reported adverse effects, even those that led to discontinuations in the trial, are well within the risk tolerance of these boys and their families. Given the choice between enduring injection site reactions and continuing progression toward death, they choose the former. Given the choice between the need to monitor LFTs and progression toward death, they choose the former.

Given the impracticability of running another clinical trial, the benefit:risk assessment must include a consideration of the risks of doing nothing. The robust natural history data (a large proportion of the total Barth population are included) demonstrate the inevitability of continued deterioration. How many parents have had to bury their boys because the standard of care is doing nothing more than managing symptoms?

In summary, I ask you to listen carefully to the experts who stand up at the microphone during the Public Comment session. You are the experts in regulatory science and regulatory flexibility. Listen to their stories and turn them into data. Listen to their stories and let them frame the question. Listen to their stories and compare them with the evidence from the clinical trials – are they consistent?

Looking at the totality of the evidence, I encourage you to judge elamipretide favorably and do so quickly. Time is life.

Sincerely,
Kevin W Freiert

Joanna Gattuso
Community Member

In October 2020 my son Alexander was born. Unbeknownst to myself he would have a severe rare genetic disease that would alter his life and our families forever. At only 5 weeks old he went into heart failure suffering from cardiomyopathy. After genetic testing we learned he suffered from Barth syndrome, a mitochondrial disease that impacts all the muscles of the body, most importantly the heart. There are a variety of limitations and obstacles he faces daily. These include the inability to eat orally (he receives nutrition and medication via a feeding tube), chronic fatigue, making him unable to keep up with his peers and physically limiting his daily activities. Smaller stature and slower growth giving him the appearance of being much younger than his peers. Other illnesses from developing neutropenia. There are no therapies that allow him to improve his quality of life. As it is such a rare disease, the trials criteria needs to take a per capita approach since the population is so small. We sincerely hope that the FDA takes into account the limitations we have as being such a small community. These therapies are crucial to improving the lives for the men and children effected by this disease.

Steven Graessle
Community Member

My name is Steve. I am a 38-year-old from Kentucky living with an ultra-rare disease called Barth Syndrome. Growing up with Barth Syndrome was extremely difficult and affects many of my daily activities. I suffered from delayed puberty and failure to thrive which meant I was physically many years behind my friends. To this day the severe muscle weakness and debilitating fatigue forces me to stop after two or three steps so my body can rest and regain my breath. The heaviness I feel in my legs after a few steps is equivalent to walking hours with ankle weights.

I want to get to the heart of the matter: my cardiology issues. On December 21st, 2013 my world came to a halt. I had developed atrial fibrillation. I did not get to spend my time enjoying my holidays with family and friends. Instead I spent it with doctor's appointment, bleeding complications, severe abdominal pain and recovering from a cardioversion. I started on cardiac medications at 14 years old and had various changes throughout my lifetime. In January of 2023 my quality of life began to deteriorate. An ECHO showed my heart function was at the lowest reading in 20 years. A cardiologist started me on new medications with a follow up appointment each month to adjust medications and dosage. The medication results are short lived in improving my function, only lasting a few months until requiring additional changes to improve my function. Since they are not specifically targeted for Barth Syndrome, we are putting tape over the cracks in the aquarium glass as the break continues to spread. Fast forward to today, I am on 10 different medications for my cardiomyopathy and heart function. In the past 8 months I had two additional episodes of atrial fibrillation and two additional cardioversions – one procedure and one medicinally with Amiodarone – which once again brought on internal bleeding, severe abdominal pain and acute congestive heart failure as determined by a BNP level at fifteen times the normal level.

In my professional life, I work in a field called Medicare Risk Adjust. This is a program that evaluates the complexity of a patient's conditions and the future cost of that patient. They ask the question, "What is the risk this patient will have increased costs and can those be reduced through other measures?" I look at the costs associated with my personal life taking 10 medications, atrial fibrillation three times, two cardioversions and weigh that to my future. A future whose next steps are more invasive procedures like defibrillators and heart transplants. A targeted medication has the potential to limit this risk.

Although not being able to physically keep up with my friends prohibited me from playing any sports, watching sports has still been a major part of my life. Barth Syndrome makes you a permanent spectator in the game of life. Watching every second pass by, watching every minute pass by, every play pass by and watching every year of what short amount of life I have living with an ultra-rare disease go by without ever being able to come off the bench to compete. A few years ago, the late NBA Analyst Craig Sager said the following during his acceptance speech of the Jim Valvano perseverance award, "Time cannot be bought, it is not wagered with God and is not in endless supply. Time is simply how you live your life." I have dreamed of a time I could go hiking. A time I could ride a bike. I have dreamed of a time I could walk up a flight of stairs without getting exhausted. I have dreamed of a time I could play and run around in the backyard with my nieces and nephews without having to give up after three minutes. I have dreamed of a time where I did not have to say no to joining my friends invites because I knew I would not have the energy or stamina to walk a long distance. A time where I did not feel like I was slowing everyone else down because I cannot keep up with the pace. I have dreamed of a time where everyone did not have to help me with everything including carrying my bags or mowing a lawn. These are all dreams not attainable living with Barth Syndrome. I dream of a time all of this will become reality.

Sara Greene
Community Member

To the FDA Advisory Committee,

Thank you for taking the time to learn about my family's struggle with Barth syndrome, and it's devastating effects. It is my sincere hope that elamipretide will be approved and more people with Barth syndrome will survive and thrive.

Our son was born in 2009 after a healthy pregnancy. They placed my newborn in my arms, only to realize he was blue. Soon he stopped breathing, and we watched a nurse bag and start CPR on our precious newborn. He coded twice within his first few hours of life.

At six days old we got a diagnosis of Barth syndrome, and he would need a heart transplant to survive. Words cannot express our gratitude for our donor family. They gave us their baby's heart to save our baby's life. We were in the hospital for six straight months. There are many children with Barth syndrome who die each year waiting on a heart.

Our son does not have a normal life expectancy, as transplants are not a cure. I can't help but wonder if elamipretide could have saved his old heart. The possibility of not outliving your own child is something I do not wish on anyone

At 15, he has grown into an empathic, kind, faithful, Braves-obsessed teenager. We are so very thankful that he survived, and we get to be his parents.

He does still have significant struggles though. He doesn't have adequate energy or muscle tone to keep up with his peers on the playground. He can no longer play in his baseball league, and has lost several friendships because he can't play the way they can. We use an adult size stroller because he simply does not have the strength to walk long distances.

This summer he wanted to go to an overnight camp. There is no way he could walk around the large campus, so I had to go to drive him around in a golf cart. It is not cool to need your mom to go with you to summer camp.

The possibility of having another baby with Barth syndrome has greatly affected our family-planning decisions. Should elamipretide be approved, we would feel much more comfortable growing our family. Barth syndrome would no longer be a fatal diagnosis.

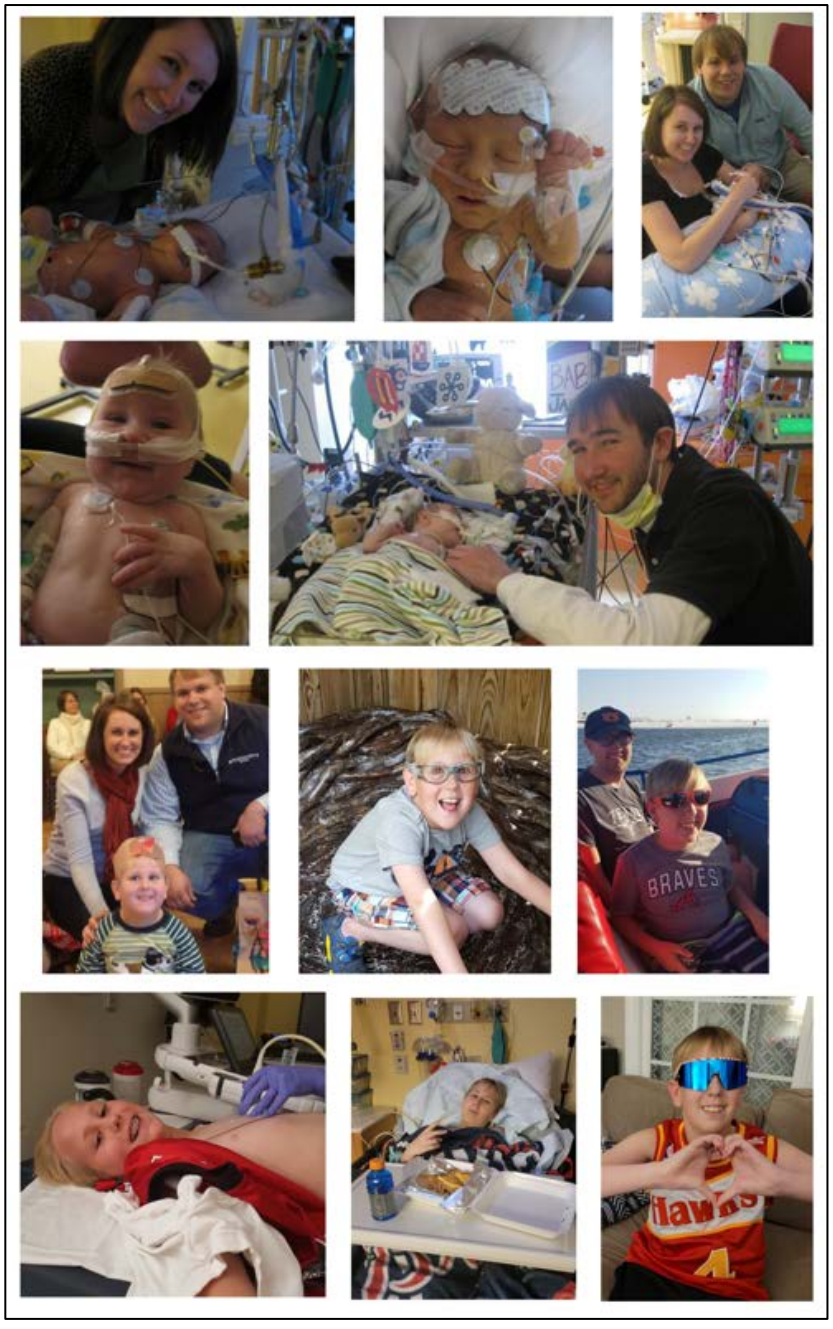
Our family considers elamipretide a miracle medication. My own brother has participated in the drug trial for seven years. He describes the treatment as life changing. Since starting the medication, he is living life, not just going through the motions. Quite frankly, he has rid the nickname of "Oscar the Grouch".

While he is looking forward to sharing his testimony with you in person, it comes down to not wanting to go on living without the drug. If he must come off the drug, our family will put him on ongoing suicide watch.

The Barth community is NOT large, but we do matter, my son matters, my brother matters- if it was your child or your brother, they would matter too.

Please approve this drug so more people with Barth syndrome can survive and live full, happy lives.

Sincerely,
Sara Greene



Marcia Hall
Community Member

Request for Approval of ELAMIPRETIDE for the use in Barth's Syndrome:

To Whom it May Concern:

My nephew, Abram Drake, was diagnosed with Barth Syndrome shortly after he was born 16 years ago. My brother and sister-in-law at the time were beside themselves with all the medical issues that came along with the diagnosis. Abram was in and out of the hospital for minor things like the common cold because he could not fight it off. He was too weak. This was my first nephew/niece, and my family was so excited to smother him in love, but because of his medical issues we hardly ever saw him. His parents were so worried about taking him out into public and him getting sick that they isolated themselves from anyone around them. My nephew was born in April and his parents were so new to the diagnosis that by Christmas time when my sister, mother and I went to pick up my adopted niece from Haiti we were not allowed to see him or spend time with our new nephew until May of that next year to ensure we were not bringing back any diseases from the foreign country. This was recommended by his doctor. The stress that has put on my family is enormous.

It was even worse when COVID-19 hit, and we did not see them for over a year and a half due to Abram's low immunity and daily exhaustion. Along with COVID this further isolation brought on depression for Abram, and he had not one friend. About a year after COVID ended my mom broke her back. Due to her age, she had other issues from this that caused her to pass away. I can count on two hands the number of times my mom saw Abram due to his poor health.

Abram is now older, and this disease is really affecting his mental health as well. He is a teenager without friends. He can't go to school without wearing a mask and has a scooter that he rides around because he does not have the strength to walk on his own or even complete a full day of school. I just want him to live the best life and if there is something that can help him do that, I will do whatever I can to get it approved. He is a teenager now and this is the time his body changes so much. This is a scary time for the family and Abram. His growth spurts can cause issues with his weakened heart. We know that the life expectancy for a boy with Barth Syndrome is much shorter than the average lifespan. I want those boys to be able to have hope for their future.

Thank you for taking my letter into consideration. I would request that the drug, elamipretide, be approved to help these boys have a chance at a normal life.

Sincerely,
Marcia Hall, Abram Hall's Aunt

Greg Holly
Community Member

My wife, Keli, and I lost a son at fourteen (14) months of age, back in 2003. He had an undiagnosed disease that ultimately lead to his death from cardiomyopathy complications. Throughout his short life, he was treated by some of the best medical professionals, including those at Texas Children's Hospital in Houston, but his disease was never diagnosed. Even through multiple autopsy efforts in labs across the nation, it was only determined that he apparently had some form of mitochondrial disease.

Having had six other healthy children, and desiring to have another child, our doctors advised us that the problem with Caleb was unlikely to happen again. We were encouraged to move forward if we wished.

Keli became pregnant again, but at the same time she continued to research and study the symptoms that Caleb had exhibited, hoping to find an answer. With no medical training, and limited experience in online research, she ultimately identified what she believed to be the root problem - an ultra rare condition called Barth Syndrome.

We were able to have a lab in New York test some of Caleb's tissue that had been preserved. The results were conclusive. He had Barth Syndrome, a condition we quickly learned was one that almost always causes the death of affected, undiagnosed boys before their second birthday. We were at once relieved (at knowing the cause of our tragic loss) and also terrified (at knowing the unborn child Keli was carrying could potentially face the same fate).

When Keli was far enough along in her pregnancy, the doctors drew amniotic fluid, grew the cells, and tested them for Barth Syndrome. Sure enough, Ben had the disease as well.

We immediately engaged a pediatric cardiologist in Lubbock, who continued to see Ben until he turned 18 years of age. He’s now seen by primary care doctors, a cardiologist and a hematologist. He takes pills and shots on a daily basis.

Ben is now almost 20 years old, and lives daily with the complications of Barth Syndrome. The cardiac issues are addressed with ongoing care and cardiac medications. The daily issues, though, have more to do with his very low immune system and his fatigue / muscle weakness.

Once we knew about the disease, and Ben's diagnosis, we joined the Barth Syndrome Foundation (BSF). The foundation serves as a support system for the families and affected individuals, and also has been the primary fundraising source for research into the disease and potential therapies.

Over the years, our small group has funded numerous research efforts. Of course, we're looking first for therapies that improve quality of life, and then ultimately for a cure to this horrible genetic disease.

Finally, these efforts culminated in the identification of a drug - Elamipretide - which was being used in other applications and appeared that it might be helpful to individuals with Barth Syndrome.

Ben began the drug trial at Johns Hopkins about 6 years ago, and has continued to take the drug to this day. He takes injections several times a week. During the clinical trial itself, he and Keli regularly traveled from Texas to Baltimore, Maryland to meet with the researchers and medical professionals to evaluate his progress and collect data.

Ben experienced significant improvement in the relief of his fatigue and muscle issues. As a result, while he continued to homeschool (due to his frequent illnesses that prevented him from attending public school), he worked at our local golf course for about four years and has now begun a missions program at a Bible

college. He still gets tired easily, and has to self regulate, but the improvement has been obvious to him and everyone else.

We've paid the ultimate price with this disease. We've lost one child, and we have another that suffers daily. Now that we finally have research and data that seems to support a therapy that improves quality of life for these young men, including Ben, we want him to be able to continue to receive this medication. People with ultra rare diseases should not be denied the right to therapies simply because there aren't thousands of individuals available for testing.

April Hubbard
Community Member

April Hubbard
113 Deerfield Drive
Painesville, OH 44077
April.driesse@gmail.com
(216) 456-6464
9/25/2024

Dear FDA Cardiovascular and Renal Drugs Advisory Committee,

My name is April Hubbard. I am a 35-year-old patient who lives with rare disease(s). I am diagnosed with a rare Mitochondrial Disease called IARS2.
I also have Primary Mitochondrial Myopathy. I am also diagnosed with Liver Hepatopathy, which is a direct result of my Mitochondrial Disease.

IARS2 is an abbreviation for a fancy long word known as Isoleucyl-TRNA Synthetase 2. It is a part of a group of Mitochondrial Genes known as ARS. Mitochondrial ARS genes are a family of genes that cause a variety of neurodegenerative disorders in the body. Each gene is an ultra-rare type of Mitochondrial Disease.

Just as there are different types of cancers, there are many kinds of Mitochondrial Disease. There are over 300 genes that cause various types of Mito, and there are 20 Mito ARS genes. All ARS2 genes are progressive and neurodegenerative.

Because of my Mito and my diagnosis of Primary Mitochondrial Myopathy, I was eligible for the study for a medication called elamipretide. I inject a trial medicine once a week into my bloodstream to help my muscles function. On Sundays, it gives me so much energy! I love it. The medication elamipretide has given me my quality of life back in ways I never thought were possible. I was bedridden and wasting away before this trial medicine. Why is this relevant?

As I mentioned earlier, over 300 genes cause various types of Mito. One of them is the one you're sitting in a meeting today to discuss the medicine I am taking for a different form of Mito, known as Barth syndrome.

I want to focus on Barth syndrome now since that is what this meeting is about.

Barth syndrome is rare. It causes weakened and enlarged hearts (a condition known as dilated cardiomyopathy), weakness in muscles used for movement (skeletal myopathy), recurrent infections due to small numbers of white blood cells, and short stature. Barth syndrome is almost exclusive to males.

I met a family on social media who have/had two sons impacted by this disease. The family is based out of Flagstaff, AZ. They have a little boy named Lukas, who is living, and another deceased boy named Zeke. Both boys had Barth syndrome.

The cruelest irony about Barth syndrome is how deceptively healthy those who have it may appear. A casual observer would never appreciate them having such a devastating illness.

Lukas is diagnosed with Dilated Cardiomyopathy, Hypotonia, Hypoglycemia and Chronic Neutropenia. Lukas is 1 in 250 worldwide who is impacted by this condition.

Lukas is an overcomer. He doesn't let his condition impact him, but it took TEN days to realize something was wrong before he was diagnosed with cardiomyopathy. The family had NO IDEA. Lukas also gets sick often, and he picks up illnesses that most people do not. This is due to

the neutropenia or low white blood cell counts. The Neutropenia can drop to life-threatening levels, and he is severely immunocompromised.

The thing about Lukas is you can look at him, and he seems normal outside, but on the inside his little heart is working hard. His legs hurt, and his muscles are working hard. He is fighting to do things that ordinary people cannot do. And what's worse?

The family lost Zeke to Barth syndrome. He was just too sick. At less than a week old, there were no options for him. His family now lives with such grief that it is such a hard thing to bear.

The trial medicine I take that treats my Mitochondrial Myopathy is a game changer for those who have Barth syndrome. Treatment with elamipretide has been found to improve organ function, skeletal muscle, heart failure, acute kidney injury, neurodegeneration, and diseases of the eye.

The treatment of cardiomyopathy in patients with Barth syndrome generally follows that for heart failure patients, including angiotensin-converting enzyme (ACE) inhibitors, angiotensin II receptor blockers, beta-blockers, and/or diuretics. However, if you approve of elamipretide, you could allow for a treatment that would be a game changer for Barth syndrome patients.

Elamipretide could be a game changer that people living with Barth syndrome and heart disease need.

Rare is expensive, and Barth syndrome is expensive. This drug could improve the quality of life for Barth syndrome and other Mitochondrial Disease patients. I am asking you to consider the quality of life of people around you and people living with Mito.

Thank you for your time.

Regards,

April-Marie Hubbard
april.driesse@gmail.com
(216) 456-6464

Brie Kalapasev
Community Member

When Milosh was born, he immediately went into heart failure. Milosh spent the next nine months in cardiac ICU fighting for his life. He made it home for his first Christmas and birthday, but his heart continued failing so much that Milosh was put on a mechanical heart and lungs and listed for a transplant. At 14 months he received his first heart transplant. By the time Milosh was three, he had spent more than half of his life in the hospital. Due to rejection issues, Milosh was put on a transplant waiting list for the second time, and he received his gift of life just before his 8th birthday. That was 6 years ago and today he is currently doing well with his second transplanted heart.

In addition to the transplanted medical life, Milosh also has Barth syndrome issues to deal with; he suffers from severe chronic fatigue and low muscle tone. He uses a wheelchair daily to move between classes at school or cover any greater than 50 feet in distance. When he goes beyond these limits, it will take him at least a full day to recover and bounce back. A two-hour visit to the park, even while in his wheelchair, will leave him completely exhausted for the rest of the day, and often the next day as well.

He can't run, jump or play like the rest of his friends. This takes a toll on his life, in every possible aspect, physically, cognitively and emotionally. Because of his physical limitations, he can't participate in regular school activities, and is often left out, missing out on chances to make connections with his peers. The physical toll of Barth syndrome is also affecting his psychological well-being; he has no friends at school.

The financial burden of having a child with Barth syndrome, coupled with two heart transplants is immense. And so is the psychological toll it adds to us, as his parents and caregivers. Milosh's mother can not work outside the home because of his frequent medical appointments and illnesses. Taking care of a medically fragile child is more than a full time job. Everything must be on time and run smoothly, from twice daily timed transplant meds to making sure health insurance coverage and specialty prescription coverages are all running smoothly. Any issue that may cause delay would put Milosh in deathly danger within days.

Elamipretide would be a life changer for Milosh's physical and psychological health. He would be able to have more stamina, but more importantly, he would be able to recover and regain energy faster.

We are hopeful and optimistic for a treatment that could help our son. Please allow him the opportunity to participate in life.

Elamipretide could offer our son a chance to finally experience and participate fully in life. Thank you for your consideration.

Jamie Loe
Community Member

To the FDA Advisory Committee,

My name is Jamie Loe, mother of 5 year son Grayson who has Barth Syndrome. From the outside he looks perfectly fine and normal, just on the small side. He just reached a weight of 29 pounds and height 36 inches tall, which is below the 5th percentile for his age. His biggest struggles are cyclical neutropenia and muscle fatigue. He is closely monitored for heart functions and does have some abnormalities. His physicians have concerns this could quickly change.

Grayson was diagnosed with Barth at the age of 2 years old. Here are just a few of the ways our lives have been impacted in the 3 years since we have received his diagnosis:

- Hospital stays are fairly normal and routine. On average he has 4 stays a year, if we are lucky. This is hard not only for him but the family that is at home. Even at his age he knows when it is time to go and sometimes will even ask, knowing he will receive multiple pokes (IVs)and have to stay.

- The fatigue is out of this world. Here are just a few examples: o He is not strong enough most days to get on the school bus by himself. While this does not bother him at his age now for us to carry him up the steps, it will soon.
    - He cannot eat a full meal without stopping due to getting to tired, when he gets tired he starts to choke or gag due to trouble swallowing. When eating at a public setting you need to scope out where the closest door or restroom is incase he starts to gag while eating. Although we rarely go out in public since he typically has no immune system.
    - If you plan a family day out, on top of planning how to keep him from wearing down you need to plan for at least two days of rest for him afterwards to hopefully prevent a hospital stay. Most times there will still be a hospital stay afterwards.
    - He cannot walk down the school hallways without tiring so we are looking at ways to accommodate that. While there is going to be a solution for that, as he ages I am sure that he will struggle with acceptance from peers.
    - He struggles to even hold a crayon or marker to color. He has to switch hands.

- He is not strong enough to attend preschool fulltime. Currently he attends 2 days a week. From 8am to 11am. He is completely physically exhausted after this. Our concerns is the impact fatigue will have on his education as he gets older.
- His conditions and level of exhaustion can change so quickly. In 30 minutes he can go from playing to you be packing your bag for a hospital stay. Just a common cold can do this.
- The number of gatherings with family and friends that we have missed out on in the short time of the diagnosis is heart breaking. We have missed 1st day of school, numerous family birthday parties and holiday gatherings, plans that have been canceled last minute are countless. We have been to the emergency room on 2 of 2 family vacations and typically have to leave early knowing a hospital stay is coming. This is with planning vacations that are low key and can get him extra rest. His body just tires so easily.

While we strive to manage what to do and what not to do, we wonder how all this is impacting him mentally especially as he grows older? When he realizes why we do not do things others do will he blame himself, will he struggle with depression? The list goes on and on. The impact of Barth does not stop with the patient. It is financially, physically and emotionally draining for all.

While there is currently no cure or treatment for Barth Syndrome, we are very hopeful for the approval of Elamipretide. We encourage the approval of Elamipretide to help lift some of the burdens and struggles and to offer a higher quality of life for those impacted by Barth Syndrome.

The Loe Family

Amanda Maksin
Community Member

Dear Advisory Board,
I am writing to you today on behalf of my family, who is personally affected by Barth Syndrome. My son Wyatt is 16 and living with the dreadful disease called Barth Syndrome. Barth Syndrome is not something that wll go away, it is something that Wyatt will struggle with for the rest of his life.

Now that he is 16 we see how the challenges of living with this have changed over the years. He obviously now is much more aware of his health. He has said that he finds it hard to go to sleep at night because of the fear of not waking up. He feels peers don't want to be friends with him because they are embarrassed of him. He has expressed concern on what will happen to him as he gets older and we are no longer here to help him. This is not something any 16 year old should be worrying about. He should be thinking of college, friends, football games, school dances, etc. , but he isn't because Barth Syndrome has robbed him of these normal experiences. Wyatts biggest struggles at this stage in his life is the unrelenting fatigue he experiences every single day and Neutropenia. It is heartbreaking watching a teenager need help standing from the couch because it hurts and he is too exhausted to do it himself. It is not fair that he has to manage his weeks by seeing what is most important to get done. He can't do anything fun without being affected by it the following day. If we go to the mall and he has to walk a distance, mind you this is with taking breaks he will pay for it later. It can drain him to the point where he sleeps the entire next day out of pure exhaustion. I have awoken at night to the sounds of him saying ow and moaning in pain. He is unaware of this, but to be in so much discomfort that you are crying out in your sleep is so unbelievably sad.

We know that Barth Syndome is a daily threat. We know that in a blink of an eye out of nowhere that his condition can take a turn for the worse. We know that the likelihood of Wyatts heart failure returning is probable. It is terrifying to imagine what it may be like to have to wait for someone elses life to end for Wyatts to continue. We have lost so many boys and men to this disease. So many of the people we met who were affected with Barth Syndrome back in 2008 are no longer with us. He sees this, we see this, and it is a brutal reality we live each and every single day. To have Elamipretide out there and not be able to have access to it is unacceptable. It has been shown in several cases with Barth Syndrome to make a huge impact. To have something available that could help save his life should we need it, or be able to help him with his daily living struggles would be life changing. We are a small community, Barth is an ultra rare disease that needs your consideration. We need your help, we are asking that you give these boys and men a chance living as normal of a life as possible. You could make a difference and be the reason these boys don't just exist and get by, but thrive.
Thank you,
Amanda Maksin

David Mann
Community Member

FDA-2024-N-3969 Open Public Hearing Elamipretide/Barth Syndrome
Hello, My name is David Mann. My son, Ben has Barth syndrome.

As a parent, I will say that there is, and always will be, a continuing helpless feeling in my gut, that our Ben will live his life with the debilitation that Barth Syndrome has dealt him. I have no control over Ben's future, but now I have new hope that the opportunity to continue the use of Elamipretide will improve his quality of life.

Ben has struggled with multiple medical issues since he was born. He struggled with daily tasks which included everything from playing with friends to playing sports when he was young, Ben could not do these things because of his weakened heart, muscle weakness, excessive fatigue and recurring hospital stays. There is so much that Ben, as well as other affected boys have suffered with their entire life.

Ben is now 27, and over the years, his health and well-being has continued to decline. Ben's health and well-being has been a roller coaster of treatments and prescriptive modifications to keep him alive.

This past year, Ben was hospitalized with heart failure and a stroke. He was released from the hospital in 'weak condition' and is now trying to recover. Soon after, Ben and his cardiologist asked the FDA for emergency use of daily Elamipretide. Ben started daily Elamipretide injections a little over 4 months ago. Since then, I have noticed that he has a definite increase in energy and has less physical fatigue. He can do more now than before he started the medication. His appetite has improved, and his overall mental wellness has also improved. I don't know if Ben realizes how much

Elamipretide has improved his health and well-being, but my wife and I see it on a daily basis. He goes fishing, now he wants to get in the pool, and he is not in bed as much as he was before starting Elamipretide. These things that I see may not seem like much to you, but I firmly believe that Ben's quality of life has taken a turn for the better since he started the daily injections.

As a dad suffering with my son's daily health issues, I ask that you please consider the possibilities of how this medication can be, and has been, a life changing opportunity for the improvement of Ben's health and future. Each young infant, each young man, and each adult man affected with Barth Syndrome, deserves the opportunity to have this medication that could be life changing for him and his family. I ask that you approve Elamipretide for use in Barth syndrome.

Sheila Mann
Community Member

FDA-2024-N-3969 Open Public Hearing on October 10, 2024 Elamipretide/Barth Syndrome

Dear Advisory Committee, I am the mother of a Barth syndrome individual, named Ben, who has suffered with this horrific disease for 27 years now. Myself, my husband and Ben's sister have all suffered emotionally and cried along with Ben. My mother and both of my sisters have suffered and lost their boys (3) to Barth syndrome. Barth syndrome has affected every aspect of our life since Ben was born. Finding out that our family had a rare genetic disease was devastating, but did give our family answers about our male deaths.

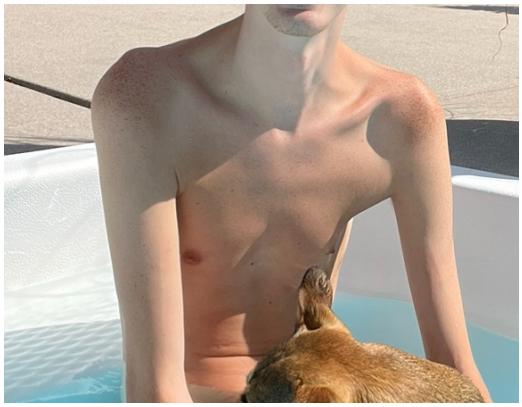
Heart failure at 3 weeks of age and being told our boy would not live to be 1 was a parent's worst nightmare. Ben has endured needles, poking, prodding, echo's, EKG, MRI's, a lifetime of feeding issues, muscle wasting, muscle pain, neutropenia, being made fun of because of his size, couldn't keep up with peers, Bullied, depression. Watching Ben witness other Barth boys die from the same disease is just gut-wrenching for a parent. And to see the Fear in his eyes is tragic.

Hearing your child tell you that he knows he will die soon is absolutely Horrifying. Those are words you never want to hear, but that is what Ben told me this past year after he suffered a stroke, and a 2nd hospital stay with severe heart failure. He came home wearing a Cardiac Life Vest. His Barth syndrome symptoms progressed to the point that he was staying in bed all day. Severe fatigue, worse muscle pain, exhaustion, muscle wasting, dropped down to 90 lbs. and 6ft 1 inch tall. BMI of 14.2. No appetite. Heart function declined back to EF 15%. Docters were discussing Heart Transplant and ICD placement. He was having to use a wheelchair just for outings and appointments. His life evolved completely around Barth.

We knew of the Elamipretide Trial, that BSF was instrumental in, that allowed Barth individuals use of the drug. Ben and I desperately ask our cardiologist to apply for emergency Compassionate use from the FDA. Ben wants to live and keep his natural heart. We want to keep our son. Ben deserves a treatment specific for Barth syndrome to give him a better quality of life. After waiting 4 months Ben was approved for use of Elamipretide.

Ben began the injections and has been on the drug for almost 5 months. Ben does say the injections are uncomfortable but has continued them daily. His father and I have already seen changes in his energy level and appetite. He has gained some weight back and is up to 110 lbs. He is out of bed more and joins us downstairs for most family meals. He is doing some cooking for himself again. He has drove his car and shopped for us at grocery store a few times and has gone hiking with us as well. Ben has come out to our pool to hang out with friends again. These are things he hasn't done in over a year and half now. He is doing some cardiac rehab exercise, per his Dr request. His heart function has improved on his last echo to EF 30%. His trabeculations (non-compaction) changed from severe to only moderate now. His tricuspid regurgitation has gone from severe to mild now. His heart and muscles are responding and improving.

The Elamipretide has improved his quality of life. We see improvements! Ben is up doing things again. Ben is smiling again. Ben is not as scared as before! Ben has HOPE! We, his parents, have HOPE! I Ask for Elamipretide to be Approved for Permanent use for the treatment of Barth syndrome. Our Son and All Affected Barth Individuals Deserve this medication to help Improve Their Quality of Life! Thank You, Shelia Mann



Kristen Maxwell
Community Member

Dear FDA Review Committee,

My name is Kristen Maxwell and I have the pleasure of caring for, loving on, teaching, and helping Hope's parents raise her over the last 3 years. Before becoming the caretaker for Hope, I owned a childcare business for over 30 years and have been blessed to care for hundreds of children. Now, I am the full-time caretaker for Hope, and I am truly blessed and so grateful to be a part of the family's life and to be chosen to care for, love, to teach and help raise our precious little Hopie. She touches hearts wherever she goes and is loved by all.

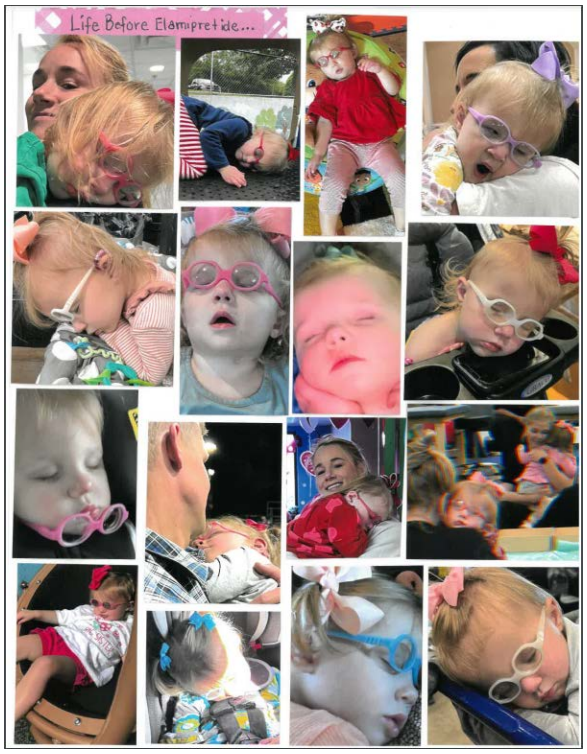
Hope was born with MLS (Microphthalmia with linear skin defects) Syndrome. MLS syndrome is extremely rare and is lethal in males. In Hope's case, this syndrome caused her to be born with many health issues including blindness, deafness, Agenesis of Corpus Callosum, and 2 heart conditions, which are cardiomyopathy and Wolff Parkinson White syndrome. After Hope was born, doctors began to prepare Hope's family to not expect her to crawl, walk, talk, see, hear, or to ever feed herself. However, over time, this determined little girl would prove these doctors wrong. We began a variety of therapy sessions, when Hope was only 9 weeks old, and little by little, day by day, we began to see improvements in many areas and to this day, we can continue doing the same.

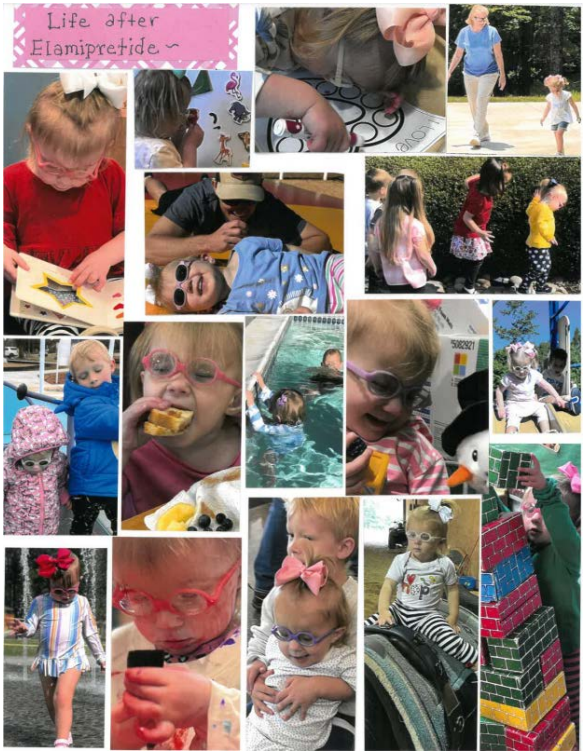
Despite being told Hope would more than likely have major challenges, we did not back down or let this discourage us but rather continued to seek out other options, opinions, alternatives, a specific diet of foods that help her body to thrive, all types of therapies possible, different, new and trial medications and different specialists for each of Hope's needs. Over time, Hope has overcome many challenges and continues to do so each day. Knowing now this medication has been documented with proven results to help maintain and improve the heart function in these children, every child should have the opportunity to benefit from Elamipretide. You, and this committee, hold these children's lives in your hands. Your decision will factor into their quality of life and even possibly if they live or die. Please consider each of these precious children's lives as your own, as your family, friends and loved ones and make the decision based on the proven scientific results.

Over the past 8 months that Hope has used this trial medication, myself, her parents, family, friends, fellow church members, teachers and therapists have seen first-hand the improvements in Hope's overall health and in the quality of life that she has gained since benefitting from this medication. Her little body has shown visible signs and documented medical proof that this medication is working to maintain and improve her life in many aspects. As I am Hope's primary caregiver, I am fortunate enough to spend a tremendous amount of time with her and can see vast differences in her daily abilities, performance and in her quality of life before she began taking Elamipretide and since she has been using this medication. Before the use of this medication, Hope would sleep most mornings often until nearly lunch time. When I would wake her up, she would cry and only wanted to be held and rocked while falling back asleep. The word that comes to mind to best describe this period is lethargic, which is not what anyone wants to witness in a toddler that should be running, jumping, climbing, playing with friends, being mischievous and making messes. With her sleeping as often as she was, she would miss snacks and meals, which in return would decrease her energy level and was not healthy for her body that desperately needed certain foods on an hourly basis. If we ever ran an errand, she would often fall asleep on the floor, in a shopping cart, in her stroller, in her seat while eating a meal or snack, in her car seat, etc.

Since she has been on the Elamipretide, she wakes up much earlier, will eat 3 meals a day with several snacks, and is able to attend preschool and participate in whatever the class is doing for the entire time, and most days now does not nap. Hope loves books and anything that lights up, makes sounds or music. She loves to play outside, to go on walks, to smell flowers, to swing, climb up and down any play structure, play in the grass or dirt, in water. She is able to enjoy all of these things now as she was not before. Having

a background for over 30 years in working with small children, both typically developing as well as those with special needs, I am very familiar with age-appropriate skills, behavior, activity levels, abilities, social aspects, what children can do at each age, etc. I have seen Hope struggle from birth, being delayed in several areas of development whether physical, neurological or intellectual standpoint. However, if Hope's precious little heart can maintain functioning at its current level, she will continue to excel. Please do not take away her potential to live life with a functioning heart. Hope has always been blessed with a huge village of support filled with more love than you could imagine. She has an older brother that she loves to wrestle, play with outside, or follow behind whatever he is doing. She will also become a big sister in February. She has been blessed with an amazing team of specialists here at home, at CHOA, in Boston, and at CHOP that are wonderful and genuinely have her best interests at heart. Part of her village now includes your panel and the decision to approve this medication that has proven to be effective in maintaining heart function in so many children, including Hope. I urge you, plead with you and beg for your mercy in making the right decision by approving this medication, placing value on each individual and potentially saving these precious children's lives. With great regards and much appreciation, Kristen Maxwell





Susan McCormack
Community Member

My name is Susan McCormack and I am writing on behalf of my husband, Ken Marra, and myself. We have two daughters, aged 20 and 18. Our daughters were conceived with the assistance of an egg donor who was unaware she was a carrier for a genetic condition called Barth syndrome. Our younger daughter was diagnosed as a carrier for Barth before she was born. Our older daughter has not been tested yet.

Our egg donor donated to two other families, culminating in the birth of five boys, three of whom have Barth syndrome. Our three families have been in contact through the Barth Syndrome Foundation since our children were quite young and we refer to these five boys as our daughters' brothers. Over the years, we have all grown close and care about each other deeply.

As our younger daughter has grown, she has delved into her carrier status more intensely and has expressed her concerns to us. She realizes that although she can't get Barth syndrome herself, if she gives birth to a son, there is a 50% chance he will be born with Barth syndrome. She has told us that she doesn't know if she could handle having a child born with a devastating condition who might die before her. She has seen how Barth syndrome has affected her three brothers and says that she doesn't want her child to have to face issues such as growth delays, constant exhaustion, difficulties eating and digesting food, frequent infections, heart disorders and even the potential for needing at least one heart transplant.

As her parents, we also fear the repercussions if she has a son with Barth, given that there are currently no treatments for the condition. Having been involved with the Barth Syndrome Foundation for over 20 years, we have watched powerlessly as the children of our extended family and friends have battled this terrible disease. We have repeatedly prayed for babies born with weakened hearts, young boys in ICUs fighting sepsis, and those awaiting heart transplants, some of which have not arrived in time. We have attended several funerals, one for a child under age 10. A little white coffin at the front of a church is an image imprinted on our hearts and minds forever.

Our immediate family has been fortunate in that our daughters' three brothers qualified for participation in the trial for the experimental drug elamipretide. They have been on the drug for several years and the results have been life-changing for them. They have made it through adolescence, a typically perilous period for the well-being of Barth individuals, relatively unscathed. They have been able to graduate from high school, enjoy time with friends and even attend college and hold down jobs. **Without elamipretide, we are quite sure that these accomplishments would have been extremely difficult, if not impossible.**

As you review the data and listen to the experts talk about Barth syndrome in relation to elamipretide, I beg you to please keep our family in mind. **We are terrified that if elamipretide does not get approved, the quality of life of our daughters' brothers with Barth will decline substantially, potentially leading to the loss of one or more of them. The devastation this would cause to all of us would be immeasurable.**

Brian McDade
Community Member

My name is James Brian McDade, I am 43 years old and a Barth patient. Because of how much they are still learning about this rare disease, I went undiagnosed until recently but it doesn't mean that I haven't suffered the effects in my youth.

I was born and kept in ICU the first three weeks of my life for Myocarditis Cardiomyopathy
I had congestive heart failure at 14 where my EF rate was 18.
I had an electro cath done at 18 where I had a V Tach on the table and they opted to install a Defibrillator
For the next 22 years I can give countless examples of the skeletal myopathy and not being able to build muscle mass, of having fatigue just walking around and yearly cardiologist appointments and device appointments just to make sure I stayed "normal".
Normal for me was never seeing a number higher than 40 for my ejection fraction rate. I have lived my entire life in what is considered "heart failure"
I had a Ventricular Tachycardia while driving my car at 40 years old and we did a subsequent left ventricle cath to asses my heart function and for now are pushing a transplant down the road.

While I have a decent quality of life, I get exhausted walking two flights of stairs (I'm not fat, I am 5' 11" and weigh 153lbs) but I cannot build muscle or increase my stamia no matter how much I work out and try to eat right. - This is Barth Syndrome

I know we are a small group of individuals but I also believe there are a lot more of us but the testing is just not there yet. But regardless we all want what everyone wants.....to feel normal, to have energy, to not have to sit out on life if there is legitimate help out there.

Thank you for listening to my story (I can give much more but was asked to hit highlights) please consider what this treatment will mean for us and if not for the few of us who are lucky enough to live as long as I have, consider what it means for the kids. A chance that they don't have to deal with all the situations I did just because not enough was known to have a viable treatment option for us.

Thank you kindly and be well.

Kate Mitchner
Community Member

To the FDA Advisory Committee,

My name is Kate Michener. My son Bryn has Barth Syndrome. Bryn is nearly 13 years old but is the average height of a 9-year-old. He weighs 60 pounds, which is two pounds LESS than his 7-year-old brother, who is unaffected. Bryn's life has been severely impacted by having Barth Syndrome. He lacks enough energy to properly feed himself so he requires a feeding tube. He gets about one-third of his daily calories through an overnight feed. His muscle weakness means he is slow, awkward and tires very easily. Bryn can't easily socialize with his peers, as he can't ride a bike, swim, run, play soccer or even walk at a steady pace for more than about two minutes.

Bryn attends public middle school and struggles with having enough energy to make it through the day. He uses so much energy simply walking down the halls that he is often too tired to learn. His school provided him with a mobility scooter to help him conserve energy. The scooter has helped with his energy levels but it has a psychological cost.

Every day, Bryn shrugs off comments of "scooter boy" from kids in the hallways. Every day, Bryn watches his younger brother running around and says, "how does he have so much energy? It's not fair." Every day, Bryn watches his friends play sports that he can't participate in. Every day, Bryn goes to a study hall instead of joining his friends in PE.

As his parent, every day, I have to watch him struggle with simple tasks that many of us take for granted, like taking a shower, brushing teeth, and getting on and off the bus with a backpack. Every night I stay up late to give him his tube feed while he sleeps. Every doctor visit, I wonder if his heart function will have decreased. I worry constantly about his physical and mental health.

In a world that struggles to make accommodations for people with only a single type of disability, having multiple disabilities often means you are on the outside looking in. As a parent, I want Bryn to be able to participate in activities with his friends. Every day, Bryn feels more and more disconnected. Every day, he feels more and more hopeless.

Bryn and I are asking you to give him a chance to have hope. A treatment for Barth Syndrome will give him hope. Hope is what he needs right now to feel like he can make connections, move beyond "surviving" and actually have a chance to "live."

Thank you,Kate Michener

Laura Nelson
Community Member

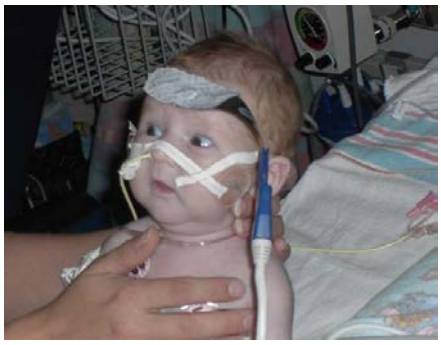
My name is Laura and my son's name is Henry. We were shocked to find out when he was a baby that he had an ultra-rare disease, Barth Syndrome. We had high hopes of sports, academics, adventure, and a long, full life for our son that most parents have. Within 1 week of the discovery of his health problems, our dreams were crushed. We were told to be hopeful that some people are able to live a long life – even 30 years – after a heart transplant. I did not consider 30 years a very long life for my sweet baby who seemed perfectly healthy 1 week earlier. We've learned a lot about Barth Syndrome and the many severe symptoms a(ecting heart function, muscle tone, energy, feeding, mobility, learning, and speech. We are heartbroken to see the older boys (teens and 20s) struggle to enjoy life with the energy sapped out of them, and there are not many people who live beyond this age. We are terrified when we think about the future for our son (now 7) and how there is no treatment currently approved to help him. It feels hopeless to be part of such a small group that nothing can or will ever be done to help us. The debilitating fatigue seems to lead to depression in a good portion of our population, and this breaks my heart. I don't want my sweet, happy son to have the energy of a 90-year-old when he's just starting out life. I have seen the results of this study, and desperately hope that we will be able to try this drug for our son.

Thank you,
Laura

Kristi Pena

Community Member

I would like my son Christopher to have the chance to try the medicine Elamipretide as we have never been given any hope or options in improving his quality and longevity of life. He has live under hospice, three bouts of heart failure, a stroke seizures and so we know the risks of life and death. We would very much like the chance to try and we know the risks (which have been proven to be minimal) we understand that it's so rare that we don't have the usual required data buy for those who exist in this world, they have given very promising results and considering the rarity of the disease we are pleading with you to take this into consideration for him and the others suffering every day with this horrible life threatening condition called Barth syndrome. Please help us prevent any more loss of life or suffering of these precious souls. To the world they may only be one person, but to us that one person is our world.



Laurie Shepard
Community Member

Dear Cardiovascular and Renal Drugs Advisory Committee,

My name is Laurie Shepherd and I live in Virginia. 38 years ago our family was blessed with our son Paul, a healthy baby boy. In the early weeks of Paul's life he was slow to gain weight and at 4 months old stopped gaining weight. Several approaches were taken to correct this but none of the doctors could understand what Paul's health issue was. By the age of 6 1/2 months Paul went into heart failure and died after two weeks of no answers in the Pediatric Intensive Care Unit at The Medical of Virginia (now VCU Hospital). His death diagnosis was Cardiomyopathy.

I am now blessed to be the grandmother of my daughter's beautiful baby boy, Owen. Owen is 10 months old and at birth developed Metabolic Acidosis. After two weeks in the Newborn Intensive Care Unit at VCU Hospital Owen's genetic testing showed that he had Barth Syndrome. With this diagnosis we now know what our son Paul died of.

Owen is currently on Enalapril to help with his cardiac ejection fraction as well as growth hormones to help with his production of Neutrophils. His weight is lower than a typical healthy 10 month old and he is slower with his developmental skills. It is our hope and prayer that the FDA will approve the forward production of Elamipretide which has proven to be so extremely helpful with the boys and men that have been able to be on it.

In addition, we have another daughter who has done genetic testing and she is a carrier of Barth as well. She has not had children yet, but hopes to one day. The knowledge of Elamipretide being available would bring her some hope in the event she were to have a child with Barth Syndrome or a child who might be a carrier.

I know I probably don't have to share the emotional and financial burden of this disease, but our daughter has had to stop working for a while because it was recommended that Owen not attend daycare until his Neutrophils stabilize. This continues to be an ongoing battle. All of this adds more emotional and financial stress and worry to the existing stress and worry of the disease.

Thank you for your time in reading this letter and for the work you are doing towards helping people with this rare disease have the opportunity to receive the treatment they need to live a heathier and more normal life.

Sincerely,
Laurie Shepher

Anonymous
Community Member

Dear Sir/Madam,

My family has a long and unfortunate history with what we now know to be Barth Syndrome. I have lost 3 uncles, a cousin and a brother, and it has caused generations of grief. My son was diagnosed in 1999. He went into heart failure at 9 weeks of age and heart transplant was considered.

As an infant he grew extremely slowly, met milestones very late, and was a 'floppy baby'. I had to be up numerous times a night to ensure medications were given, and due to heart failure, he would feed every 40mins and then need to rest. He was unable to attend daycare as he was so unwell and vulnerable and I was unable to work.

As a toddler he was very small and weak. He didn't walk until he was nearly 2 years of age and he would struggle to get up from the floor without assistance. He would get knocked over and tire easily. As he grew (very slowly) and had more active days, which would be far less active than his peers, he would scream at night due to the pain in his legs from lactic acid build up. He would then be exhausted for the next few days and we would be unable to leave the house. This set the pattern for how we had to plan days and manage pain and the sheer exhaustion he would experience after.

Many accommodations were required for school. He would fatigue trying to write with a pencil/pen, he would fatigue trying to learn and retain the information. He also struggled with friendships as he would be unable to keep up with friends in the school yard. He required a place he could take frequent breaks. He had a lot of school absences and required extra assistance. To enable him to attend school excursions I had to attend. Again I was unable to work.

Psychologically Barth Syndrome significantly impacted my son. He struggled to maintain friendships as he couldn't keep up, was too tired on weekends to socialize or take part in limited extra-curricular activities. He wasn't invited to friends homes as parents were worried about the responsibility of caring for him. By the time he was 10 years old he had already lost several very close friends to Barth Syndrome. These boys were of similar age or not much older, something children of his age shouldn't have to experience. He was very aware of being different and suffered noticeable anxiety from 7 years of age. Despite seeking help, this developed into anxiety induced Tourettes Syndrome, which isolated him further. This also impacted his siblings, father and myself. The whole family has been significantly impacted, emotionally, socially and financially by this disease.

As a teenager he had a very limited social life, again due to weakness, fatigue and pain. He required a mobility scooter to assist with moving around middle/high school and carry books. Due to the educational load, fatigue, pain, infection, and chronic diarrhoea and lack of bowel control, he had extensive time off of school. He required an extra year to complete high school and graduate with a high school certificate. His very limited energy and weakness inhibited him from catching the school bus and we needed to be available to drop him off and pick him up from school, again limiting our ability to work. His brother got in to trouble protecting him from bullies and he and his sister's missed out on so much as we were unable to take them places as a family in consideration of his brother's disability and financial burdens.

He is now 25, and has worked hard to achieve his degree and works as a high school teacher. He is unable to work more than 4 days per week and has no social life as he is exhausted when he gets home. He wants to be a contributing member of society but tells me he feels weaker and more fatigued with each year. This impacts his earning ability, where and how his able to live, and he has huge concerns for his future, both financially and socially. He expresses this as living inside the body of an 80 year old. He is worried about being a burden. A treatment for Barth Syndrome could enable him to maintain the energy he has now, continue to work and possibly have the social life he would dearly love. Thank you for taking the time to read my submission.

Erin Swieton
Community Member

Dear FDA, Thank you for allowing our voices to be heard. I appreciate all that you do to protect our lives, securing safety for medications and treatments. Pease understand that the Barth Syndrome community is small by the nature of it being an ultra rare disease. Despite this, our sons continue to struggle and suffer from the effects of Barth Syndrome, specifically fatigue while waiting for a life saving treatment. Elamipretide could be a life saving treatment for our son, medically and lifestyle speaking.

In a sense you've grown up with my son while I have shared with you about how Barth syndrome has wreaked havoc on him and our family. I've heard from those who have taken Elamipretide that it has literally given the life of independence and normalcy to those with Barth Syndrome. I know that there is concern about Elamipretide being a risk to the health of our sons, and I'd agree. However, for us, the real risk, is Barth Syndrome itself. It is devastating families, including ours. I beg you to please listen to our plea and understand the positive effect this medication has had on a few and could have on our lives.

The fatigue felt by my son is often referred to as "Barth Tired," a level of exhaustion that most people cannot comprehend. It is a debilitating disease that has the power to knock out any sense of normalcy in families. It's so intense that my son struggles to meet his own basic needs as a growing child who should be able to care for himself in full. As a comparison, he is less independent than his elementary aged siblings, who do not have Barth Syndrome but face challenges like ADHD that effects their executive functioning. Still, they surpass his independence.

I worry daily whether my son will make it to school today, or be too fatigued. He misses 30% of his school days and can only go part-time. If he makes it to school, I worry that he may not make it to Physics class because he's too exhausted to walk down the school hall from Band class. This is not a far walk and other students are doing this without concern. My son has access to an electric scooter at school but wants to be like his peers on his feet. We are considering him taking a day off mid week to recuperate from school. Walking his classes exhausts him and the mental fatigue effects his concentration and ability to absorb instruction. Therefore, he works harder than most to obtain a GPA of over 3.5. I'm a very proud mom.

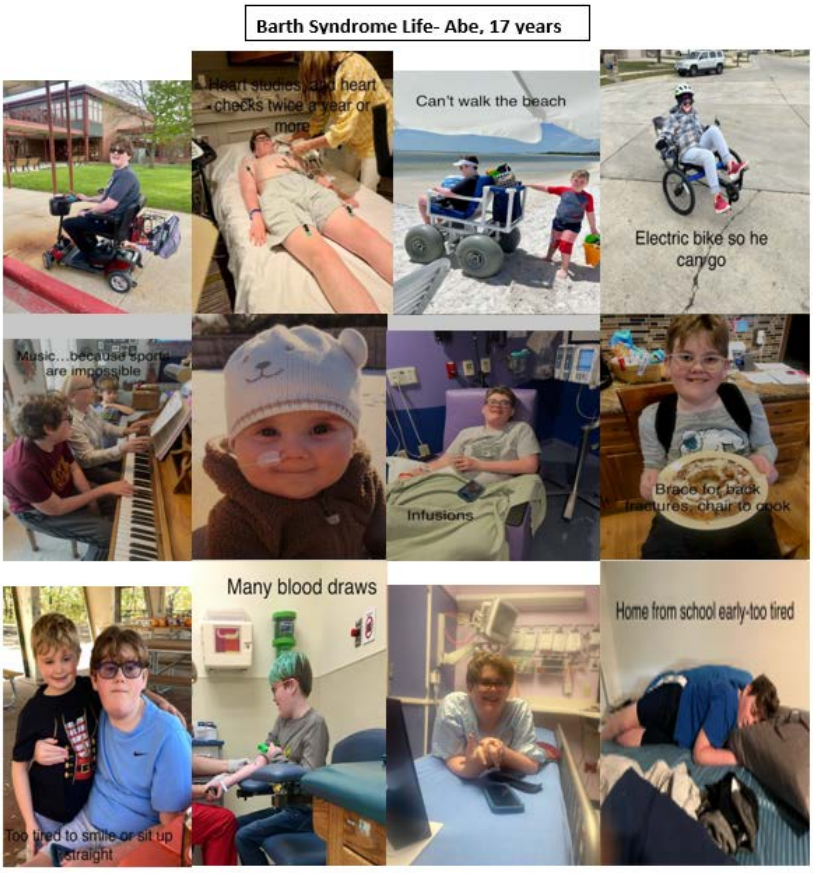
We think about college. Achieving his degree likely will take up to ten years due to his limited energy, which will prevent him from studying more than one or two classes at a time. Unlike his peers who find jobs, he faces the risk of unemployment, especially undesirable employment, and must navigate a Vocational Rehab program to identify his strengths and find supportive employers willing to hire individuals with disabilities. His friends choose their job from a list of desired options, who then apply and often employed without a class or assistance like my son. This last summer my son had his first job, he worked two hour intervals three times a week, unable to do more than this. Happily though, he felt so much pride and purpose from this position at a local thrift store who hire many people with disabilities.

As for me, I wake up forced to have flexibility in my day. I don't know if I will need to pick up my son from school prematurely, cancel my plans for the day, call on others to help with the other children in our family, cancel work to tend to my teenage son with Barth Syndrome. Many things do not get done in our home because of Barth Syndrome fatigue. Even finding the time to keep up our household is difficult

because of the attention my son requires. It's not uncommon for him and our family to miss outings, events, or parties because of his fatigue. These are the daily realities he faces, and we face as a family. Nothing can be certain. The only certainty is with fatigue from Barth Syndrome.

Despite striving for normalcy. Planning and attempting to live life in a meaningful and engaged way, it's sad to say that inconsistency and the burden of Barth Syndrome is our normal. It has become what we can expect with Barth Syndrome in our family. My son is at a pivotal point in his life where he is able to realize the burden his fatigue and inability to be independent causes. He has mental health issues stemming from not being able to care for himself, feeling too tired too often, feeling as though he is a burden, and finding it difficult to be like other peers and therefore make friends. This is because of Barth Syndrome fatigue.

I understand elamipretide is a risk, but hopefully you can hear that so is Barth Syndrome. The risk to my son's independence, the risk to further illness, the risk to decreasing mental health, the risk to obtaining an educational degree, the risk to function as a contributing member of society, the risk to our family's normalcy. This is an intelligent, persistent, tenacious man who is cognitively capable to contribute, with great potential. But his body limits him. His life can change with elamipretide and he wants to try it in hopes to better engage with the world and share his talents, skills, and empathic nature. He is truly worth it. The world needs more of my son, and he deserves more from the world. Otherwise, really, our risk remains as Barth Syndrome. At this point what do we have to loose?



This is a snippet of Abe's life with Barth Syndrome. We try to enrich and make life the fullest it can be for him, but always with an undertow of fatigue and accommodations, and disappointment isn't unheard of because Abe is too tired. The fatigue and endless medical care effect his life, and his family's life, tremendously. We need a treatment so he can participate in life and feel good in it. Thank you. – Erin, Abe's Mom

Quan Tran
Community Member

An Uncle from Vietnam Dear FDA, I am writing to you as a concerned uncle of a young boy, Nhat, who has been diagnosed with Barth Syndrome. Nhat was born in 2016 but was not diagnosed with Barth Syndrome until November 2022 after experiencing serious dilated cardiomyopathy. Nhat's journey with Barth Syndrome has been a profound challenge for our family. I vividly recall the distressing moment when Nhat was rushed to the Emergency Unit with his heart barely functioning, his EF plummeting to 12.5%. The toll on our family was immense, with my sister collapsing and my mother developing an anxiety disorder that she continues to manage with medication. While Nhat has shown remarkable resilience and returned to school after a year-long hiatus, his daily life is fraught with obstacles. His persistent fatigue and inability to engage in physical activities have isolated him from the joys of childhood. He can't play any sports with his friends at school, or even climbing 1 staircase will require him a few stops to rest. His vulnerability to illnesses continues to instill fear in our family. Recently in June 2024, he had to admit to hospital for 22 days due to severe pneumonia. The looming specter of dilated cardiomyopathy poses an ongoing threat. With his heart's EF hovering around 32%-36%, the uncertainty of his future health weighs heavily on us. The prospect of a heart transplant remains out of reach due to his current condition and limitations in Vietnam's health system, leaving us with a sense of helplessness. Every day is a battle for Nhat's life, and it pains me that our ability to help him is limited to prayers. It is in this context that I implore the FDA to prioritize the review of elamipretide for the treatment of Barth Syndrome. As a beacon of hope that has demonstrated significant promise in clinical trials, elamipretide represents a potential lifeline for Nhat and others affected by Barth Syndrome worldwide. The expedited review of elamipretide is not merely a medical necessity but a deeply personal plea for our family. I firmly believe that accelerating the review process for elamipretide is crucial in addressing the unmet medical needs of individuals with Barth Syndrome, offering a ray of hope to patients and families, including my own. I am deeply grateful for your attention to this matter and for your unwavering commitment to advancing the review of treatments for rare diseases.

Sincerely, Quan Tran

Picture of Nhat and me when he got Dilated Cardiomyopathy and later diagnosed with Barth Syndrome in November 2022

Pictures of Nhat and his friends on the Opening School Day this September 2024 (Nhat is way smaller than his classmates despite he is 1 year older)

Peter Van Loo
Community Member

Dear members of the Advisory Committee,

My name is Peter van Loo, I am 37 years old, live in the Netherlands and was diagnosed with Barth Syndrome at the age of two. The core symptoms that have always affected me the most are chronic fatigue and muscle weakness, though these indirectly lead to several other issues.

The first years of my life were relatively normal with only minor adaptations, but that changed when I went to university. I had to move out of my parents' house and do my own housekeeping, cooking, etc., all while the study load increased drastically. I struggled to follow 1/3 of the curriculum, which was the minimum the university was able to let me do. I still missed too many lectures to pass most subjects in one go and had to join a different group of students every year as my study mates moved on more quickly, even without me joining any clubs or associations.

It took me 7 very lonely years to complete my propaedeutic year, which drove me into severe depression. When I realized I wouldn't be able to obtain a bachelor's degree that way, thankfully a student counselor saw potential in me and helped me write a resume based on my personality and natural talents rather than education, which helped me get several part-time jobs.

Each attempt of 3-4 hours a day for 3 days a week went well at first but started to burn me out after half a year to a year. After a decade of stubbornly trying, failing, recovering, trying again and failing once more, I decided to apply for full disability allowance and being exempt from looking for work, which was granted despite extremely strict rules around that. Since then, my life consists almost entirely of chores at home (even with the help of a housekeeper) and online social interactions. I don't have the energy for much more than that.

My body naturally found ways to cope with the disease, which weren't necessarily the best. Using muscles for my posture was too exhausting, so I always heavily leaned on my skeleton: hanging on my spine, locking my knees every step, not "bothering" with aligning my legs with my ankles. That saved a lot of energy at first but lead to scoliosis and damaging my joints. Now I have chronic pain and often need braces to support my back, ankles, knees and hips to even move around the house.

Lastly there are also significant financial implications. My income is of course limited to disability allowance, which is only 75% of the minimum wage for a fulltime job in my country. I need better healthcare insurance than most people which comes with higher premiums, e.g. for extra dental coverage because brushing my teeth is too exhausting to pull off three times a day. My limited energy also makes me rely more on deliveries vs store visits, precut ingredients vs fresh ones, etc. All that is more expensive too.

Elamipretide may not solve or prevent all these issues completely, but I believe a moderate improvement in energy and muscle strength could still reduce my social isolation and make me more financially independent. If others get access to this treatment earlier in life, it could postpone chronic pain by many years and prevent loneliness and financial worries altogether.

This letter only covered a fraction of how Barth Syndrome affects me and how elamipretide could have helped earlier and still can. The full picture could easily have filled five pages on each element, but I didn't have the energy for that because, you know…

I hope this has been insightful enough in its summarized form regardless though. Thank you for taking this medication into consideration and reading this information.

Peter van Loo

Julia Vanderhart
Community Member

My brother, Walker, and nephew, Jackson, have Barth Syndrome, and I am a genetic carrier of the disorder.

My brother is 34 years old. For 27 years, Barth Syndrome controlled everything he did. The improvements that he has seen in his strength, energy and quality of life for the past years is something he could only dream about before. Because of the study drug he does not have to dream about it. Thankfully, It is his reality.

He was diagnosed with cardiomyopathy and low muscle tone as an infant. It took until he was nineteen years old to get a diagnosis of Barth syndrome.

His heart size and function returned to the normal range during his childhood but his energy level and muscle tone remained low.

Growing up, he participated in Boy Scouts, earning his Eagle. Some physical activities, such as hiking, had to be modified to meet his needs. he was driven around at summer camp to save his limited energy. When walking, he had to stop and rest two or three times every 1⁄4 mile. After a week at camp, it took several days staying home to recover. After graduating from college, he has been able to work full-time, but he had no energy to do anything else. Imagine your twenties without energy to do anything beyond work.

In August of 2017 he unrolled in the TAZPOWER study, and immediately enrolled in the open label extension after the blind portion of the study was complete. His daily life is so different than just a few years ago. We used to call him Oscar the Grouch because he was always out energy. As his little sister, I thought all boys had to go to the doctor as frequently as Walker did. It was not until I was older to realize the toll it was taking on him.

Now he has this vigor for life and his body is no longer holding him back. It makes me emotional to think how much and how long he was suffering without us, his family, realizing it. When people ask if he has Barth syndrome, Walker says “No, I had Barth Syndrome”.

I think about my 15 year old nephew, Jackson, who is limited by Barth syndrome. It is so hard to watch his self-esteem dwindle as he realizes these limitations. I hope one day he is given the chance to find relief and can have this blossoming I have seen in my brother.

Thank you for your time and consideration.

Josie Van Londen
Community Member

Dear FDA Committee,

I am writing to share my personal experience with elamipretide, which has been nothing short of transformative for me. I have been on this medication for over two years, currently through a compassionate release supply.

Before starting elamipretide, I had great difficulty with basic tasks such as turning over in bed and getting dressed. These activities were exhausting, and I was becoming more dependent on others for assistance. Since beginning elamipretide, I have regained almost complete independence in my activities of daily living (ADLs)—a remarkable improvement that has vastly enhanced my quality of life.

As a medically retired physician, I deeply appreciate the value of effective treatments, and I am concerned about what will happen if I lose access to this medication. Without elamipretide, I fear that I will regress more quickly, potentially losing the independence I have worked so hard to regain. To be frank, I believe that without elamipretide, I might not even be alive today.

It's also worth noting that the side effects I have experienced from elamipretide have been minimal, especially in comparison to the profound benefits it has provided.

Thank you for your time and attention to this critical matter.

Sincerely,

G [Josie] van Londen, MD, MS

Amy Wald
Community Member

WALD FAMILY TESTIMONY FDA 2024 (NDA) 215244

I am writing to you on behalf of my incredible son, Levi. Levi was born on March 30, 2012 and it was the happiest day of our lives. My husband and I were overjoyed to welcome a baby boy into the world. Everything seemed perfect until the next morning when we expected to take Levi home, but instead, we were sent to the Neonatal Intensive Care Unit (NICU) at Children's Hospital of Wisconsin.

Levi stayed in the NICU for over a month while doctors struggled to diagnose his condition. After consultations with specialists across the country, we finally received a devastating diagnosis: Barth Syndrome (BTHS).

Levi is now 12 years old, and while he has received excellent care. His life is a daily struggle. He has been on four medications since the first month of his life, and while these medicines help keep his heart functioning, they come with harsh side effects. Levi still wets the bed every night due to the medication, and at 12, this affects his self-esteem and social life. Sleepovers have become a source of embarrassment for him, and he is often exhausted in the mornings, making it hard to get him out of bed so we peel him out of his bed.

Levi loves sports, especially baseball. Last year, he was voted MVP of his team, excelling as a pitcher—the one position he can play despite his muscle weakness. However, his condition severely limits his ability to run, causing him to stumble and slow down significantly. It breaks my heart to watch him struggle to do what he loves. Recently, Levi was so exhausted after a critical game that he couldn't even play in the championship match the next day. As he grows older, his stamina is declining, and I fear that soon, even baseball—the one thing he loves most—will be taken away from him.

Basketball is another sport Levi enjoys, though he can no longer participate actively. The coaches kindly allow him to sit on the bench and wear the team jersey, just to be part of something he loves. This year, however, he won't be able to join at all because his body simply can't keep up.

Two years ago, Levi's dream came true when he met his hero, JJ Watt, through the Make-A-Wish Foundation. They played football together at Camp Randall Stadium, but Levi was too weak to walk on his own. At only 9 years old, he had to be carried by his father—an experience that, while unforgettable, also left him feeling deeply embarrassed.

There are so many simple joys we can't share as a family. Whether it's a walk at the zoo, a hike, or a family bike ride, Levi's lack of stamina makes these experiences impossible. Barth Syndrome has taken away more than just Levi's health—it has stolen moments of connection and normalcy that we yearn to experience together.

Levi has a younger brother and sister who love him dearly, and he often compares himself to them. He

questions why he has to take medications daily while they don't, and it breaks our hearts when he says, "I want to be normal." We live in constant fear that his heart condition could cause him to collapse at any moment, with no warning and no way to save him.
As Levi's parents, we continue to hope and pray for a treatment or cure. There is currently only one medication in development that offers hope for Levi and other boys like him—Elamipretide. Since beginning this process, 17 boys affected by Barth Syndrome have passed away. What if this drug could have saved their lives? What if Elamipretide could prevent the same fate for Levi?

During a recent visit to John Hopkins, I met with a researcher connected to the Barth Syndrome Foundation, who shared that treating Barth Syndrome is just as critical as addressing any other disease. If we can find a proven treatment, it could open the door to breakthroughs for other mitochondrial diseases, including multiple sclerosis (MS). Elamipretide represents the first real chance for not only Barth Syndrome patients but also those suffering from similar mitochondrial conditions.
We respectfully urge the FDA to conduct a fair, equitable, and comprehensive review of Elamipretide for Barth Syndrome. This drug could be life-saving for Levi and others. We ask you to consider not only the few boys with Barth Syndrome but the wider impact this medication could have on those suffering from other rare and life-threatening diseases. We remain hopeful that Elamipretide could be the answer we've been waiting for to give our son—and countless others—a fighting chance.

Jess and Jay Wiederspan

Community Member

I am writing in support of the approval of Elamipretide. As a sibling of someone affected by this devastating condition, I have witnessed firsthand the relentless decline that accompanies Barth syndrome. Watching my brother struggle daily with basic movements, like getting out of a car or rising from a chair, is heartbreaking. His body wavers unsteadily, yet he refuses help, striving to hold on to his dignity.

He adores my child and wants nothing more than to spend time with her, but his constant fatigue makes this difficult. Simple activities drain his energy, forcing him to rest for long periods. He longs to do more than just watch from the sidelines—whether it's working, socializing, or even participating in family events. But the physical toll of Barth syndrome often requires him to conserve his energy for days before and after these occasions, robbing him of the joy they should bring.

We have waited years for a treatment that could offer him and others living with Barth syndrome a chance at a better life. The potential of Elamipretide gives our family hope that he could one day experience a life with more energy and independence.

Please consider the profound impact that approving Elamipretide would have on individuals like my brother. It would not only enhance their quality of life but also bring hope to families who have been waiting for years for meaningful progress.

Thank you for your consideration.

Anonymous
Community Member, Elamipretide Trialist

I am 42 years old and have been living with Barth syndrome my entire life. I was officially diagnosed in 1991 at age nine, but the symptoms were present from birth.
Barth syndrome affects nearly every aspect of my life. I have extreme fatigue that prevents me from working. I have to carefully manage my activities throughout the day to prevent becoming overtired . It Can Take a few days to recover if I have a full day of activities.

Another major challenge is muscle weakness, particularly in my legs. Walking more than a block or two is difficult , so I rely on an electric scooter for longer distances. This weakness also causes balance issues. Stairs are particularly hard to manage. Going up, I get winded and tired quickly. Coming down, I feel unsteady and need a handrail or some kind of support. I feel as though I might fall forward when stepping onto a descending escalator. Lifting anything over 40 pounds is very difficult.

Because of the fatigue, I missed out on many normal childhood and teenage activities. After elementary school, I had to leave my peer group and attend a smaller private school instead of the large public middle school my sibling attended. By the time I reached high school, I was homeschooled because I had difficulty keeping up. After High School I started a two-year degree program that took me nine years to complete.

I was fortunate to take part in the Elamipretide trial, but unfortunately, my time on the drug was cut short, which likely prevented me from experiencing the positive effects that many of my Barth brothers felt. I was on the drug during the initial phase, then taken off, and later placed back on during the open-label extension (OLE). After a few months on the OLE, I had a bad injection site reaction, and Stealth decided to discontinue my participation due to safety concerns. Despite this, I would have gladly continued taking the drug.

For those of us living with Barth syndrome, a potential treatment like Elamipretide has been a long-held dream. My hope is that those newly diagnosed won’t have to endure the same hardships I faced growing up.

While I was planning on attending the Oct.10th meeting in person, I have decided I am not able to travel.

Thank you for your time.

Anonymous
Community Member

I am writing as the mother of a son with Barth syndrome, an ultra rare genetic disorder that has profoundly impacted his life since birth. Barth syndrome is a cruel and relentless thief, continuously robbing those affected of possibilities, opportunities, independence, and dreams for the future. My son's journey with Barth syndrome illustrates its devastating effects:

1. Education: He barely managed elementary and middle school, requiring daily tube feedings and battling extreme fatigue. High school was completed via homeschooling, with many days lost to exhaustion. It took him 6 years to complete a two-year degree from a local community college.
2. Career: Despite his intelligence and determination, he cannot work due to debilitating fatigue. He set up a small business based on his two-year degree after graduating, but had to stop because of his muscle weakness and fatigue. Most painfully, Barth syndrome stole his ultimate dreams of joining the military or becoming a pilot.
3. Social life: Unable to attend school normally past elementary grades, he has limited friendships outside the virtual Barth syndrome community. As a result, some of his closest friends have had their lives cut short by this merciless condition. These losses are stark reminders of the deadly nature of Barth syndrome, and the grief of losing friends compounds the challenges he already faces. Despite this, he continues to face each day with courage and determination.
4. Health: He has endured numerous hospitalizations, relies on an ICD to prevent fatal arrhythmias, takes multiple heart failure medications, and suffers from severe neutropenia, osteoporosis, and depression.
5. Mobility and quality of life: His progressive muscle weakness now requires a power wheelchair for anything beyond short distances, limiting his mobility. He struggles with his balance and stairs are very difficult. Any family trip or outing demands extensive planning, accommodations, and recovery time, but we always ensure he can participate and would never leave him behind.
6. Independence and dignity: He faces multiple indignities due to his increasing muscle weakness—for example, sometimes being unable to stand up from a seated position or get out of a chair without assistance.

Despite these challenges, my son is extraordinary – kind, generous, thoughtful, positive, funny, and smart. He manages his complex medical regimens independently and volunteers remotely with the Barth Syndrome Foundation.

Now, a potential treatment – Elamipretide – offers hope to our entire Barth syndrome community. This opportunity, which we've awaited for decades, is tantalizingly close. We understand that all medications carry risks, but we also know with absolute certainty the lifelong, serious, and progressive risks of Barth syndrome. Our hope is that Elamipretide will slow or even halt the progression of Barth syndrome. For younger affected individuals and the newly diagnosed, it could mean avoiding the suffering and missed opportunities that have defined our experience.

I implore you to approve Elamipretide for the treatment of Barth syndrome. Give our beloved Barth babies, boys, and men the chance to fight back against this merciless condition. Their futures hang in the balance.

Amy Wilson
Community Member

I'M MOM, COUSIN, & AUNT OF BARTH AFFECTED PEOPLE.
THANK YOU FOR TAKING TIME OUT OF YOUR DAY TO BE HERE & THANK YOU FOR LISTENING TO OUR PLIGHT.

MY SON HAS ENDURED MORE IN HIS 24 YEARS OF LIFE THAN MOST HAVE BY THEIR 90S. HE'S BEEN POKED, PRODDED, TESTS, AMBULANCE RIDES, ER VISITS, AND HOSPITAL STAYS-SO MUCH SO- I'VE LOST COUNT. I'VE WATCHED HIM SEIZE AND TURN BLUE. I'VE WATCHED HIM MISS MONTHS OF SCHOOL & HAVE TO BE QUARANTINED DUE TO HIS IMMUNE SYSTEM. JUGGLING WORK, DRS APPTS, BEING A WIFE, AND TRYING TO ALSO BE THERE FOR MY OTHER SON, ALL WHILE DOING MY BEST TO KEEP MY SON ALIVE.

THESE AREN'T THE THINGS THAT SCARE ME. THIS IS MY LIFE.
IT'S BEEN A NEVER-ENDING BATTLE TO MAKE PEOPLE LISTEN, TO GET HELP.
WHAT SCARES ME IS KNOWING WITHOUT THIS MEDICATION, QUITE POSSIBLY HE'S LIVED HALF HIS LIFE. STATISTICALLY SPEAKING.

IT SCARES ME KNOWING, I MAY NEVER SEE HIM GET MARRIED.
IT SCARES ME WATCHING HIS MENTAL HEALTH DETERIORATE, ALONG WITH HIS PHYSICAL HEALTH.
BLESS HIS HEART, HE WORRIES ABOUT ME AND MY FEELINGS. MY MENTAL HEALTH.
IT SCARES ME KNOWING I WON'T HAVE GRANDCHILDREN. HE'S MADE IT ABUNDANTLY CLEAR HE WILL NOT HAVE CHILDREN. HE DOESN'T WANT TO PASS THIS DEADLY DISEASE ON.

THIS MAY CHANGE, SHOULD WE GET TREATMENT AVAILABLE.
WE'VE ENDURED MANY OBSTACLES WITH BARTH SYNDROME AND HAVE BEATEN ODDS.
WITHOUT YOUR HELP IN GETTING THIS MEDICATION, THIS TIME- WE WON'T.
I DON'T WANT TO SEE THE INSIDE OF ANY MORE AMBULANCES, ER ROOMS, HOSPITAL ROOMS. NO MORE MEMORIALS & PHOTOS OF THOSE WE CONTINUE TO LOSE. I'M SCARED I WILL HAVE TO BURY MY CHILD- SOMETHING NONE OF US SHOULD EVER HAVE TO GO THROUGH.
I'M PLEADING WITH YOU ALL TO PLEASE HELP US WITH THIS TREATMENT.

OUR NUMBERS ARE SMALL IN OUR COMMUNITY BUT WHY SHOULD WE MATTER LESS?

WHY SHOULD OUR FAMILIES BE EXCLUDED OR MATTER LESS?
I KNOW THIS MEDICATION WORKS. I'VE SEEN IT WITH MY OWN EYES. I KNOW THERE'S NO SIDE EFFECTS. I JUST WANT THE CHANCE TO WATCH MY SON, MY NEPHEW, MY COUSIN, AND THE OTHERS TRY AND LIVE A QUOTE NORMAL LIFE. I'M ASKING YOU TODAY, PLEASE HELP US.
DO WHAT'S RIGHT BY OUR COMMUNITY.
DO RIGHT BY THOSE WHO ARE SUFFERING & DYING DAILY.
THANK YOU!

Rachel Wilson
Community Member

Dear FDA Committee,

I am writing to you because the upcoming hearing for the Barth Syndrome community in regards to elamipretide is very important!

I have received elamipretide for the last nine months, and have seen substantial positive changes to my health. The intensity and frequency of my bad days has decreased. I have more better days. I am able to chew and swallow without choking. I have the ability to talk and use my mouth muscles without fatigue, instead of needing to rest my voice and limit my conversations with loved ones at the end of the day. I am able to exercise and support and increase my mitochondria. Without elamipretide, my muscle decline would have continued without reprieve – once the body stops, the body dies.

Having experienced significant improvement with elamipretide, I fear losing access to the only hope there is to halt mitochondrial disease. The withdrawal or discontinuation of this crucial medication would be devastating- it is our only hope for quality of life. There is no other equivalent bio available option, other than elamipretide. It concerns me that lack of access to this medication will lead to the elimination of proven study based favorable outcomes for patients. Thank you for your continued efforts to make elamipretide FDA approved.

Thank you for your time and compassionate concern.

Rachel Wilson

Kim Winningham
Community Member

Hi, my name is Kim and my 18 year old nephew, Luke, was diagnosed with Barth Syndrome around four years ago after years of testing. I knew at an early age that Luke was different, different in a medical way. The way Luke didn't progress like other children. Even his pale skin. He always looked sick. Luke would ride in a stroller at an older age when his younger sister would be running around full of energy. We would say he's just lazy not knowing what was really going on inside his body. The older he gets the less interested he is in things because he knows he can't physically or mentally do them because of the disease. I know kids with this don't live as long with the heart and other issues that come along with it. My nephew and I would appreciate a medication that can slow the progress of Barth Syndrome and hopefully improve his muscle strength, heart, and energy. So please give us hope and support the approval of Elamipretide as a treatment for Barth Syndrome for my nephew, Luke, and others like him. Thank you, Kimberly

Kevin Woodward
Community Member

To the FDA Advisory Committee,

The data on Elamipretide , captured and studied over eight years and two clinical trials, show minimal likelihood of risk, and potentially life-changing benefits for people living with a disease that has no treatment options. This new medicine could give my son an opportunity to live a longer, fuller, more healthy life.

My 14-year-old son, Connor, lives every day with the knowledge that he has a deadly disease with no cure. In addition to shortening his life expectancy, this disease also greatly reduces his quality of life and sets him uncomfortably apart from his peers. Because of his extreme weakness and fatigue, he is not able to do "normal" teenage activities such as riding a bike, participating in gym class, even opening a can of Coke or a bag of chips. His immune system does not produce enough white blood cells, so he cannot ward off bacterial infections – he takes injections at home to help boost his natural immunity. He misses many days of school per year for doctors' visits and illness. He lives with a permanent feeding tube that goes directly into his stomach. He isn't able to participate in organized sports. He isn't strong and coordinated enough to brush his teeth properly or even clip fingernails. He also has heart disease, and takes a number of daily cardiac medications, brings a portable AED with him everywhere, and is weighed down by the constant threat of a severe cardiac episode. He is very small compared to his peers, weighing only about 72 pounds.

Barth syndrome has affected every part of his life from the day he was born. As a newborn, he could not breathe on his own and spent five weeks in the NICU. He had difficulty eating. He missed all his physical milestones; he never crawled, and he did not walk until he was almost three years old.

Unless there is a significant advance in medical care, Barth syndrome will continue to affect all his future milestones as well. For example, we anticipate physical, social, and psychological challenges with his transition to high school. The school building is large and has multiple flights of stairs that could impede his ability to get from one class to another on time, especially while carrying a heavy book bag. His noticeable physical differences and abilities can make it difficult for him to fit in with his peers. The gravity of his situation is taking its toll on his mental health as well.

With no FDA approved therapies for people living with Barth syndrome, we were surprised and thrilled when a clinical trial for an investigational medicine, elamipretide, began. We would have done almost anything for Connor to be able to participate, but unfortunately, he did not qualify for the study due to his age and small size. But we remained hopeful that the treatment would be approved, and the progression of his Barth syndrome would be curbed – particularly as we saw others in the Barth community improve while in the study.

Our community has continued to advocate, including by delivering a petition to the FDA signed by nearly 20,000 people from all 50 states. We request that the FDA review and approve Elamipretide, using the greatest amount of flexibility possible, so patients like my son will never have the opportunity to try the only potential treatment that could change their lives.

Submitted respectfully,

Kevin G. Woodward,
kgwoodward@gmail.com
443-415-4711

Stacy Woodward
Community Member

My name is Stacey Woodward and I am mom to my 14 year-old son Connor who has Barth syndrome. Connor looks like a relatively normal, 8-year-old, but in fact, he's a 14-year-old, 72 lb teenager who is much shorter, skinnier and weaker than his middle school peers. Connor's life has been seriously impacted by having Barth syndrome.

-He cannot eat enough by mouth, and therefore has a permanent feeding tube in his stomach.

-He embarrassingly cannot make it through the night without wetting the bed because his muscles are too weak to hold his urine

-He is not strong enough to play organized sports, even though he LOVES them

-He is too weak to participate in gym, but yearns to connect with his classmates

-He cannot normally socialize with his peers because he is always fatigued and simply cannot walk as fast, ride a bike, swim, or climb stairs as quickly as they can. He cannot keep up.

-He cannot open anything. Every jar, package, even cans are brought to his parents to open.

-He does not have the fine motor skills in his hands to tie his shoes.

-He cannot brush his teeth properly and suffers from gum disease and visits to the dentist terrify him.

-He cannot properly trim his toenails and suffers from debilitating ingrown toenails.

He's literally trapped inside a body that fights against him every chance it gets. What my son can do is ask for a chance. He can ask for an opportunity to better his life in any way possible.

-He wants to be able to take a girl on a date.

-He wants to get a job.

-He wants to be able to drive a car.

He isn't asking for much. He knows any chance at a "normal" life is seemingly impossible and he knows he'll likely die early. But while he's here, he wants to LIVE. Currently, he's just waiting to die, and it literally breaks our hearts.

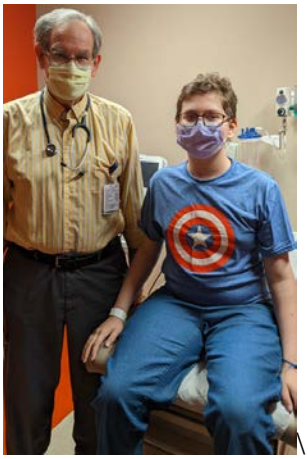
We're just asking for a better quality of life for him for the time he is here. Having access to Elamipretide could change the course of his life. Please approve Elamipretide to give Connor a chance.

Thank you.
Stacey Woodward

Eric Zeitner

Community Member

Greyson is 16 with a heart transplant of 15 years. Elamepratide could give him the life he deserves. A life where he can have a job not limited by his lack of energy due to Barth Syndrome. A life with less suffering and more well rounded fulfillment that we all spire. Please allow him and his Barth brothers the opportunities that they all deserve. We have worked very hard to get here.



Alicia Zins
Community Member

I am the parent of two male children, ages 22 and 17, with Barth Syndrome and a daughter who is wrestling with wanting to know if she carries the TAFAZZIN gene. It took almost eight years for our first son to be diagnosed with Barth Syndrome, only after our second son was born with more severe issues, requiring a lengthy NICU stay.

While it was difficult to watch both boys from infancy to preschool age struggling with feeding and developmental milestones, it was heartbreaking once they entered grade school. The struggle to navigate stairs as if they were elderly required them to be at the back of the line so other children did not get frustrated. The playground equipment was off-limits since there was not enough staff to accommodate their physical needs and ensure they did not seriously injure themselves if they fell. Their legs would buckle when jumping off a low platform and landing on their bottoms. If they did fall forward, their arms were not strong enough to stop them from hitting their face. Thus, we have had a broken nose, teeth knocked out and numerous scratches on the face due to falling.

As they moved into junior high and high school, the difference in physical abilities with peers became much more visible. For example, their running version was more of a fast walk, not a run. We quickly learned that Physical Education class was not an option due to some of the activities and because they would become extraordinarily exhausted to finish the school day. From a social perspective, sleepovers were tough, not only from a medication perspective but also the fatigue and falling asleep by 8 pm. Standing in the student section at the football games was not an option either. The crowding of the students, the jumping up and down, climbing the bleachers – all these activities were exceptionally challenging due to weakened muscle tone (they would feel “wobbly” and unsafe), especially the core muscles.

In addition, additional planning for any school event outside the classroom. For out-of-town events, I always had to tag along, due to their numerous medications and someone needing to be there for extended breaks and potential sickness. On a school trip to Epcot at Disney, they only navigated one or two rides and became extremely fatigued and nauseous, unable to complete the tour of the countries. Every extra event comes with the question – will they have enough energy for that? Can they take off the next day from school to rest if they go the night before?

This drug can ease not only the physical symptoms but also the constant worry, “Do I have enough energy?" of those suffering from Barth Syndrome. Most importantly as my daughter, contemplates testing as a carrier, getting married, and having children, it would be a huge relief to know that there is a drug that can ease the symptoms of Barth Syndrome and her children, my grandchildren, would not be faced with the same question, will I have enough energy? My daughter would have more peace as her children navigate the school day and attend after-school events.

What does our sons' future hold without this drug? Could they work a full-time job? Should they get married, or have children? Should they move to another city more than an hour from their parents? These can be questions for any parent, but for a parent of two young men with Barth Syndrome, it is

tremendously daunting. The questions then become more focused on me as an aging parent with an adult disabled child. The mental strain in planning for retirement versus care for your adult disabled child. Having relief from the physical symptoms will significantly impact their mental health as well as mine. Maintaining resilient mental health in battling a life-long rare disease is first and foremost in sustaining the course of treatment and diligence in practicing the proactive measures to stay safe and healthy.

Thank you for the opportunity to be heard. Please consider approving Elamipretide for my sons and future grandchildren.

Peyton Zins
Community Member

I am a 22-year-old male, affected with Barth Syndrome. I have a younger brother that is affected also, and a sister that is contemplating being tested as a carrier.
Living with Barth Syndrome has shaped my daily experiences in profound ways. This rare genetic condition presents a unique set of challenges that affect my physical abilities, emotional well-being, and overall quality of life. While I strive to navigate the world as best as I can, the realities of living with this syndrome often feel overwhelming, underscoring the constant balancing act between my aspirations and my limitations.

One of the most significant aspects of Barth Syndrome is its impact on my mobility and endurance. Simple activities that many take for granted become monumental tasks for me. For instance, I can only walk for about 15 minutes before I need to stop and rest. This limitation not only constrains my physical freedom but also dictates my social interactions and daily routines. For example, when I was on the golf team in high school and my condition was deteriorating, I ended up having to ride in a cart during events and even then, at times, could not complete the round. Simply navigating a busy day can quickly turn into a test of endurance and willpower. I often find myself timing my movements, calculating how much energy I have left, and trying to anticipate when I'll need to pause. This constant awareness can be exhausting and disheartening.

When I do push myself beyond my limits, the consequences can be severe. On such occasions, I often end up feeling nauseous, to the point of vomiting, and experiencing diarrhea. This has led to needing many accommodations and missing events in school. The accommodations include creating a class schedule that is the most efficient path to limit steps, but then I could not always take the classes I wanted with my friends. I often missed assemblies and sporting events because I was simply too tired or the activities were too physical. As I get older and begin my professional phase of life, I find myself having to excuse myself from important meetings when these symptoms arise, which can be frustrating and worrisome regarding how my co-workers and supervisors perceive me. Additionally, I have to make numerous accommodations for work travel and trips simply due to lack of stamina to get on the necessary early plane or car rides. I have to spend extra money for a hotel room in case I need to rest in the middle of the day. Simple site visits that my peers attend without a second thought become extremely draining for myself. In general, it is a harsh cycle: the desire to engage fully in life, paired with the very real limitations imposed by my condition.

The above reasons and many more not listed, are why I ask for approval of Elamipretide, not only myself, but for my little brother and future nephews. It would give all Barth patients a second chance at life. Specifically, it would allow me and my family freedom to do simple things like a walk in the park or a family trip overseas without constant worry and anxiousness that my body will not be able to endure the trip. Additionally, I could start to engage in my social life once again, not having to concern myself if I will be able to walk down the block to the bar without potentially fainting. Overall, it would allow me to live the life I see so many others living, a life without constant fatigue, nausea, and anxiety over mundane day to day tasks.

Medical and Scientific Expert Submissions

John Lynn Jefferies
Medical/Scientific Expert

Dear Advisory Committee Members and members of CRDAC,

We, the undersigned physicians and medical professionals, are specialists knowledgeable about the care of Barth syndrome. Currently, there are no approved treatments specifically for Barth syndrome. This letter is being submitted in support of elamipretide (docket # FDA-2024-N-3969), for which a new drug application is currently under review for the treatment specifically of Barth syndrome.

Barth syndrome (BTHS) is an ultra-rare genetic mitochondrial disease that affects fewer than 150 individuals in the United States. Barth syndrome is a devastating, life-limiting X-linked genetic disease leading, in all known cases, to early death primarily due to cardiomyopathy. Patients do not typically survive past their third decade. While the heart-associated factors of BTHS are life-threatening, affected individuals are plagued by profound and crushing fatigue caused in part by skeletal myopathy that severely limits their ability to participate in life activities such as attending school, holding a full-time job, or engaging in social activities. As individuals age, they suffer from progressive heart failure and associated progressive, debilitating skeletal muscle weakness, exercise intolerance, and fatigue which can impact ambulation and require use of mobility devices.

The BTHS community has suffered greatly and there is an urgent, unmet need for a treatment for this condition. Since 2020, the community has lost >5% of the US population. Individuals with BTHS are at risk for sudden death, particularly during infancy and adolescence. Any medication with the ability to stabilize cardiac function or improve quality of life for this population would be a significant improvement over the currently available treatments. A therapy that has the potential to delay progression or even reverse the trajectory of the disease would greatly impact this community.

The natural history of this condition has been evaluated by several research teams. In particular, left ventricular stroke volume consistently decreases over time (Chowdhury et al., Pediatric Cardiology, 2022) and exercise intolerance is pervasive (Hornby et al., Orphanet, 2019; Thompson et al., Gen Med., 2016) due to decreased mitochondrial respiration (Powers et al., Front Physiol., 2013). As patients age, they do not improve and their quality of life progressively declines.

We have reviewed the published data from SPIBA-001, a Phase 3 Natural History Control trial designed to establish a control for interventional data from SPIBA-201 Part 2, a 192+ week open label extension trial of elamipretide as a potential treatment for BTHS. Data from both these studies have been published and the results are compelling.

- Aside from injection-site reactions, no serious adverse events related to the treatment were reported.
- All functional assessments showed substantial improvement over baseline measurements including the 6-minute walk test (>25% durable improvement), fatigue assessments, muscle strength (>45% durable improvement), SWAY balance assessments and 5x sit-to-stand.
- Left ventricular stroke volume increased 45% over baseline through 168 weeks of elamipretide treatment

Importantly, from the cardiologists signatory to this letter, the significant and large improvements in left ventricular stroke volume index support a view that elamipretide has contributed to cardiac

structural remodeling in this patient population. For drugs known to have this effect, the typical time-course to early observation of the effect is typically 6-9 months, which is consistent with the trajectory of early improvements observed in this trial beginning around week 36 of the open-label extension. The magnitude of the effect **far exceeds the variability that would normally be observed in this population** and is directionally consistent across multiple time points assessed, supporting a favorable interpretation of these data.

These changes can be further contextualized clinically by meaningful changes reported by patients in their quality of life. Patients have experienced concrete improvements in their ability to participate in activities of daily living including being able to attend school and continue onto college, maintaining gainful employment, starting new businesses, travel and engaging in normal social activities.

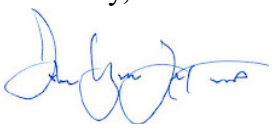
The cardiovascular clinical trialist signatories on this letter are intimately familiar with large trials in heart failure which often contain thousands of participants. While this dataset is comprised of a small number of patients, proportionate to the BTHS community size, the *changes observed are striking*.

- Sustained gains of ~100 meters walked in 6 minutes over a 4-year period in young men presenting who had Class II/III heart failure at baseline is unprecedented.

There is a known placebo effect (~30-meters on the 6-minute walk test) in heart failure trials (Olsson et al., European Heart Journal, 2005). In our clinical judgement, however, that the magnitude of change observed in this dataset far outstrips the typical placebo effect. Because these changes have been sustained for 4+ years, they cannot be attributable solely to hope bias. Moreover, the supportive findings regarding durable improvements in muscle strength and 5X sit to stand, which are extremely challenging assessments for these patients, also debunk any concerns with hope bias.

Given the progressive, life-limiting cardiac and skeletal muscle manifestations for BTHS patients, the considerable unmet need, the elamipretide open label efficacy data and safety, we want to have the opportunity to prescribe elamipretide to our patients with Barth syndrome. As mentioned above, thousands of patients cannot be enrolled in a disease population such as BTHS; these numbers simply do not exist. In conclusion, as medical providers familiar with and in many cases actively treating patients with BTHS, relying upon our best ability and medical judgment of the clinical and basic science data collected to date, we urge FDA to make a fair, equitable and appropriate review for elamipretide.

Sincerely,



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Team Cardiologist, Memphis Grizzlies

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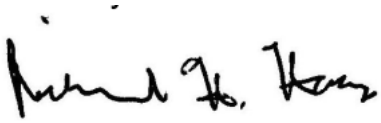

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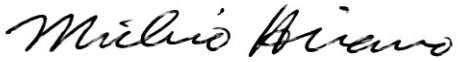
University of California San Diego, La Jolla, CA



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Dr. Patrizia Cavazzoni, Director, CDER
Food and Drug Administration
10903 New Hampshire Ave
Silver Spring, MD 20993-0002

September 6, 2024

Dear Dr. Cavazzoni

Our team has been caring for an infant born in February 2024 with Barth syndrome. The male child was able to access elamipretide therapy through an Emergency IND that Dr. Thompson in the Division of Cardiology and Nephrology at CDER promptly authorized. I am writing to thank you on behalf of our team and our patients' family for CDER's facilitation of our emergency IND request. It is our opinion that elamipretide was instrumental in successfully bridging this very ill infant to a successful transplant, and he remains on therapy post-transplant.

On March 7, 2024, we contacted the sponsor, Stealth BioTherapeutics, about our then 2-week-old male patient admitted to our NICU at UCLA with Barth Syndrome. He was in severe heart failure and was listed for heart transplant, but we were worried he would not survive the wait for transplant with his very poor cardiac function. We accordingly sought emergency access to elamipretide for his treatment. Dr. Thompson authorized the Emergency IND and the sponsor promptly shipped drug, enabling his first dose of elamipretide via IV infusion on March 14, 2024. In addition to elamipretide therapy, he also received standard heart failure medications including milrinone, carvedilol, furosemide, clonidine and heparin. This dosing regimen successfully bridged the child to his transplant on July 30, 2024.

At birth, this child was in severe heart failure and we worried he would not survive until transplant. Many children with Barth syndrome and other lethal pediatric cardiomyopathies do not survive the wait or the procedure. We fully expected to need a Berlin heart to bridge this child to transplant, which we were able to avoid. After four and a half months on elamipretide therapy, he went into the transplant procedure far healthier than we would have expected. Our team believes that elamipretide contributed to this child's overall well-being and health, enabling him to go into a transplant setting in good condition. He is now recovering rapidly, with discharge expected within a month post-transplant.

Our team recommends and the child's family desires that he stay on elamipretide post-transplant. In the setting of Barth syndrome, while transplant can alleviate the cardiac manifestations, it does not address the myopathic presentation of this devastating disease. We will be amending our patient's IND to accommodate SC administration on an outpatient basis.

We understand that elamipretide is not yet approved for the treatment of Barth syndrome. In our expert opinion, it was a critical tool in our arsenal to stabilize and support this child through transplant, and we view the potential benefit afforded by elamipretide relative to its known risks as clearly supporting a decision to make this drug immediately available to patients and prescribing physicians battling with this devastating pediatric disease. We certainly hope to have it available for our future treatment of this child and other individuals affected by this syndrome.

Thank you again for facilitating access to elamipretide.

Very truly yours,

Nancy J. Halnon, MD
Health Science Clinical Professor, Pediatrics
Division of Pediatric Cardiology
UCLA Children's Heart Center
Pediatric Heart Failure and Transplant

Cc: Dr. Robert Califf, MD
Dr. Aliza Thompson, M

Brittany Hornby
Medical/Scientific Expert

Thank you so much for the opportunity for this advisory committee. I was fortunate enough to have the opportunity to serve as the physical therapist in the Kennedy Krieger Institute Barth Syndrome clinic from 2012 to 2024. I also had the opportunity to serve as the primary physical therapist, who completed the functional assessments, for the Elamipretide clinical drug trial. From experience, that I have seen the boys and men affected by Barth Syndrome are plagued by muscle weakness, decreased functional exercise capacity from a very young age that these challenges have a significant impact on their quality of life. I was completely amazed by the Elamipretide trial results for many of the participants, as I have not seen many boys and men with Barth Syndrome who are able to walk more than 300-350 meters on a 6 minute walk test and I saw multiple individuals accomplish that (I have attached 2 of our teams papers below with additional result details). I was also blown away by the subjective comments some of the boys and men reported, for example, one individual reported "I don't feel like I have Barth Syndrome anymore." Thank you for the work of the advisory committee to hopefully help bring a medicine to this community that has the potentially to significant improve the quality of life of many people.

Additional submission:

Apologies for my multiple submissions. Following completion of my comment earlier, I felt that words and published articles did not tell the full story of the clinical drug trial that the committee is reviewing. I first want to say that to make it to this point has been the result of decades of hard work by the patients and their families, the Barth Syndrome Foundation, Dr. Hilary Vernon and Stealth BioTherapeutics. I have been lucky to be part of these efforts for the past 12 years. I have attached a presentation to provide some additional insights into the background of the Kennedy Krieger Institute Interdisciplinary Clinic and the research journey that lead us to the Elamipretide TazPower study.

Rebecca McClellan
Medical/Scientific Expert

Kennedy Krieger Institute • 707 North Broadway • Bal more, Maryland 21205 443-923-9200 *(main)* • 443-923-2645 *(TTY)* • KennedyKrieger.org

9/25/24
Dear Advisory Commitee,
I'm a certified genetic counselor at Kennedy Krieger Institute, Neurogenetics-Metabolism clinic and also with the Johns Hopkins Center for Inherited Heart Diseases. I've been in practice for 22+ years and the majority of the pa ents I work with have what would be considered a rare disease, most ultra rare like Barth syndrome. I have been working with patients and families impacted by Barth syndrome my entire career, engaging with them through our Interdisciplinary Clinic at Kennedy Krieger Institute (KKI), the only of its kind in the US, and also through work and support of the Barth Syndrome Foundation. Our clinic at KKI started in 2012 and we've formally cared for 53 individuals in that me, with countless consults to other medical providers across the country and world.

Early in my career there were very little we could offer families once a genetic diagnosis was made, the diagnosis was for knowledge and planning. But that is changing with so many new therapeutics and the promise of gene therapy, its just amazing how far science and medicine have come since I began my career. Yet sadly, much of this still lags behind for those with rare disease.

In the last few years I have been direct witness to the powerful benefits of Elamipretide from both patients taking it as an extension of the trial and from others who received it for compassionate care use.

I'd like to share two stories that I think help emphasize just how life saving this medica on can be. First, at our September 2023 clinic, the parents shared that they were unexpectedly pregnant. Two weeks later they learned the baby was an affected male with Barth syndrome. Through prenatal echocardiograms the baby was determined to have heart failure and at our urging transferred prenatal and delivery plans to their closest hospital with NICU and neonatal heart failure experience. As her due date approached, the local team used the word fu le to describe the situation and we all prepared for the worst. Shortly a er delivery, the baby was listed for transplant and compassionate care use of

Elamipretide was sought and granted. It was a long road, but the seeming miracle is that he is now home, delisted, and at our September 2024 clinic, his heart function was normal.

I contrast this story to another from a family we have followed for years. The mother reached out this summer to share that her niece, who never followed through on learning her carrier status, delivered a baby boy with severe heart failure at a local hospital. Diagnosis was delayed and sadly he passed away at just 20 days of age shortly after learning that he had Barth syndrome. I recognize that timely diagnosis is a factor here, but I think these stories also speak to the role that Elamipretide can play in saving lives if it is readily available as an adjunct to our current heart failure therapy.

Availability and development of medications that help those with rare diseases are few and far between. I share my comments today because we have lost way too many boys and men with Barth syndrome and I've

seen how much those living with the diagnosis are impacted in their daily lives. I believe if there is a medication that can help, then it should be made accessible to all who would benefit.

Rebecca McClellan, MGC, CGC
Genetic Counselor
Neurogenetics – Metabolism

Laura Ortmann
Medical/Scientific Expert

To whom it may concern:

I am the Director of Cardiac Critical Care at Children's Nebraska and am writing on behalf of our heart failure and critical care team.

Our care team at Children ' s Nebraska has been caring for an infant born earlier this year with Barth syndrome (BTHS). This young boy was provided compassionate access to elamipretide therapy through an emergency IND. We believe elamipretide was beneficial as part of the treatment regimen contributing to a positive outcome and transplant-free discharge for this gravely ill infant.

The child's mother was closely followed during her pregnancy as a confirmed carrier of BTHS with a history of multiple family members with BTHS. During the pregnancy, diagnosis of BTHS was confirmed through amniocentesis. Fetal echocardiograms during pregnancy suggested that his cardiac disease was not going to be life threatening after birth, but he became much sicker than expected and I would like to share our experience.

After birth he was immediately transferred to our hospital due to severely depressed biventricular function (LVEF - 20%). He was intubated at 1-day-old due to rising lactates and administered milrinone, calcium chloride, and epinephrine infusions for hemodynamic support. He was extubated at 6-days-old, but failed due to his severe heart dysfunction and was re-intubated. Some of his support could be weaned, but he continued to have decreased cardiac function. During this time, we were working with insurance to transfer him to a different facility for implantation of a left ventricular assist device and potential heart transplantation. Neither of these were ultimately required due to his impressive response to interventions including both standard of care therapies and elamipretide.

Elamipretide therapy was initiated at 34-days-old at 0.25 mg/kg/day IV and increased to 0.5 mg/kg/day at 39-days-old. At 36-days-old, the child also began oral heart failure medications including carvedilol and spironolactone and, at 39-days-old, captopril. Heart failure medications were titrated up over time while milrinone was titrated down and eventually discontinued at 51-days-old. Throughout his hospital course, the patient' s echocardiogram improved with normalization of right sided function and improved LV function to the low normal range. During this time, the patient also made steady progress and was able to demonstrate weight gain on all oral feeds. The patient was discharged home at 61-days-old on daily doses of elamipretide0.5mg/kg SC and an oral heart failure medication regiment.

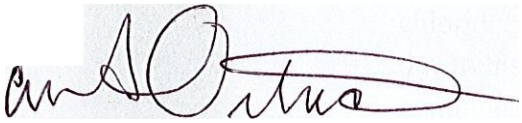
After discharge, the patient continued to maintain oral feeds and has been doing well. At 73-days-old, his echocardiogram showed improvement of LVEF to 60% (from 49% at time

of discharge). Most recently, at his 6-month vis it, his left ventricle was within normal size and is now functioning normally.

During hospitalization and outpatient follow up, his mother has reported no side effects from elamipretide . Our team has been impressed by his recovery, including a remarkable improvement in cardiac function such that the patient was never placed on the heart transplant list as originally planned.

Understanding that elamipretide is not yet approved for the treatment of Barth syndrome, we are grateful that we had the opportunity to access this investigational therapy. We cannot solely attribute his recovery to elamipretide given he was receiving other heart failure therapies at the same time, but his transition from potentially needing a hem1 transplant to having normal heart function is remarkable. Based on our experience with this one patient, we believe elamipretide can be an important addition to the resources available to treat this devastating disease and we credit its addition to the standard of care but non-disease specific treatments as contributing to a positive outcome for this young child.

We hope that elamipretide will soon be made available as a prescribable resource to treat any future patients with Barth syndrome.



Laura Ortmann, MD

Director of Cardiac Critical Care, Children's Nebraska

Patient Advocacy and Peer Organization Submissions

Barth Syndrome Foundation
Patient Advocacy

"Saving lives through education, advances in treatments, and finding a cure for Barth syndrome."

Emily Milligan, MPH
Executive Director
Barth Syndrome Foundation
2005 Palmer Avenue #1033
Larchmont, NY 10538

September 26, 2024

Submitted to docket FDA-2024-N-3969

Dear Members of the FDA Advisory Committee,

I am writing on behalf of the Barth Syndrome Foundation's Board of Directors, our staff, the families we serve who are affected by Barth syndrome, and our diverse partners and allies. We ask you to thoughtfully and thoroughly review the evidence for elamipretide, which includes the consideration of patients' voices in support of its profound impact in their lives. Having appropriately weighed these considerations, we are hopeful you will emphatically encourage the FDA to approve elamipretide as a vital treatment for people living with Barth syndrome.

Barth syndrome is an ultra-rare, life-threatening genetic disorder that profoundly impacts the lives of those affected. It leads to cardiac dysfunction, severe muscle weakness, immune issues, and debilitating fatigue. Tragically, this disease claims and alters lives – often without warning.

The unmet medical need in our community is vast. We ask you to consider the boy whose fingers are too weak to open a soda can without his parents' help. We ask you to consider the teenager who wears nighttime protection to prevent bedwetting and will never attend a sleepover because of the social implications. We ask you to consider the child who learned his primary colors not through typical childhood experiences, but through the colors of the medications he took in hopes that one of them might alleviate his Barth syndrome symptoms. We ask you to consider the countless number of children and adults who did not receive the gift of life in the form of a new heart in time.

Elamipretide has shown remarkable possibilities, demonstrating the potential to increase muscle strength by 45% and heart function by 40%. Half of the people who participated in the original clinical trial have been using this investigational therapy for nearly seven years, enduring daily injections because they recognize the treatment's value in improving their lives outweighs the sacrifice. Infants once in cardiac failure left the hospital with their native hearts much to the amazement of their physicians after being offered this experimental therapy, underscoring its critical role in their ongoing care and opportunity at a full life.

The data to date support a strong safety profile for elamipretide. Given that, **all individuals living with Barth syndrome deserve every option that modern medicine can provide, including access to elamipretide.**

Our organization is dedicated to advocating for individuals affected by Barth syndrome and ensuring equitable access to essential healthcare. Your role in reviewing life-changing therapies, such as elamipretide, is both vital and highly respected.

As you review the evidence supporting elamipretide's use for treatment of people living with Barth syndrome, we urge you to listen to our stories and consider the lives impacted by this disease and the real hope that elamipretide represents for patients and their families that they have heard about and seen in those who have been lucky enough to have had access to it. Your thorough review of all available information and the equitable and appropriate application of maximum flexibility for this very rare yet devastating disease will make a profound difference.

We thank you.

Sincerely,

Emily Milligan, MPH
Executive Director
Barth Syndrome Foundation

Children's Cardiomyopathy Foundation
Peer Organization

September 26, 2024

Submission to docket FDA-2024-N-3969

Dear Esteemed FDA Advisory Committee,

I am writing on behalf of the Children's Cardiomyopathy Foundation (CCF) to express our strong support for the approval of elamipretide for the treatment of cardiomyopathy in children, particularly in cases where the disease is linked to mitochondrial dysfunctions like Barth syndrome.

Founded in 2002, CCF is committed to improving the diagnosis, treatment, and quality of life for children affected by cardiomyopathy. Pediatric cardiomyopathy, a chronic heart disease, is one of the leading causes of heart failure and sudden cardiac arrest in children. Despite the severity of this disease, advancements in pediatric treatments have been slow, with limited therapeutic breakthroughs.

Elamipretide represents a significant opportunity to change this narrative. Early studies have demonstrated its potential to improve mitochondrial function, offering hope for children and others affected by mitochondrial-linked cardiomyopathies such as Barth syndrome. As a non-invasive therapy, elamipretide could not only prolong lives but also drastically enhance the quality of life for children with this rare form of cardiomyopathy, many of whom face heart failure and may ultimately need a heart transplant.

Currently, pediatric cardiomyopathy is estimated to impact 30,000 children in the United States, with thousands more undiagnosed. For those affected by the mitochondrial form of the disease, treatment options are particularly scarce, and families are left with a huge unmet medical need. Research has shown that elamipretide has the potential to address the root cause of these mitochondrial defects, thereby improving heart function in affected children. The potential of this drug aligns with CCF's mission to provide families and children with access to effective treatments and reduce the severity of cardiomyopathy's life-threatening consequences.

The FDA's approval of elamipretide could lead to a breakthrough in the treatment of mitochondrial- related cardiomyopathy and represent a significant leap forward for addressing children's heart diseases and saving lives.

We respectfully urge you to support elamipretide's approval. Doing so would advance a desperately needed treatment option for families and give children and others affected by this disease a chance for better health and longer lives.

Thank you for your consideration of this critical issue. We remain hopeful that with your support, elamipretide can be a potential lifeline to families in need.

Sincerely,

Lisa Yue

Lisa Yue
Founder & President of the Board

Friedreich's Ataxia Research Alliance (FARA)
Peer Organization

533 W Uwchlan Ave | Downingtown, PA 19335 | P: 484-879-6160 | F: 484-872-1402 | www.cureFA.org

Docket No. FDA-2024-N-3969 for "Cardiovascular and Renal Drugs Advisory Committee; Notice of Meeting; Establishment of a Public Docket; Request for Comments—New Drug Application 215244 for Elamipretide Hydrochloride Injection."

Comments submitted September 26, 2024

The Friedreich's Ataxia Research Alliance (FARA) is a non-profit research advocacy organization based in the United States, representing multiple stakeholders in the Friedreich ataxia and rare disease community including individuals living with these disorders, their families, researchers, and clinicians.

Friedreich Ataxia (FA) is a rare, monogenic, autosomal recessive multi-system condition that shares both pathophysiologic and clinical features with Barth syndrome. Both conditions are caused by mutations in nuclear genes that are essential for mitochondrial function.

Symptoms shared among individuals living with FA and Barth syndrome:

- serious heart conditions, including cardiomyopathy, that can lead to heart failure and early death
- loss of strength and muscle function, difficulty walking
- fatigue - energy deprivation that limits activities of daily living

FARA has been following research developments in Barth syndrome and the Barth Syndrome Foundation and FARA regularly meet to share insights. We have been closely following the clinical studies of elamipretide for the treatment of Barth syndrome as clinical improvements have been observed in cardiac function and walking are both important in FA as well.

We are encouraged that the Advisory Committee and the FDA will hear from the Barth syndrome community on October 10th, 2024, to understand the tremendous burden of disease and unmet medical needs of individuals and families living with Barth syndrome. Individuals with FA have expressed that even modest improvements in function and/or slowing of disease progression are meaningful and that individuals are willing to accept uncertainties in magnitude of clinical benefit when treatments have strong safety profiles and are well-tolerated, as the certainties of their progression due to FA (or Barth) are devastating.

We have reviewed the Natural History Control Trial designed to establish a control for interventional data from SPIBA-201 Part 2, the open label extension trial of elamipretide as a potential treatment for Barth syndrome. Taken together, the data are robust and support the use of elamipretide for Barth syndrome. In addition, we have spoken to members of the Barth syndrome community who have expressed their conviction that the benefits outweigh the risks when considering elamipretide as a treatment.

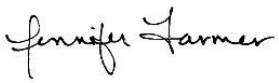
As the cardiac disease in both Barth syndrome and FA is the primary cause of early mortality, we find these results very compelling. We believe that use of stroke volume is clinically meaningful and is likely to be the only endpoint achievable. These are diseases that also affect mobility and thus standard or typical cardiac clinical endpoints are not feasible and outcomes such as survival are not acceptable or ethical given the high unmet need and the long duration required to prove such an outcome.

FARA has co-funded research with Stealth Biotherapeutics to evaluate the potential for elamipretide and other molecules such as SBT-589 to treat symptoms in FA (these studies are ongoing). We believe from the Barth syndrome clinical studies that these drugs may have benefit for a wider indication of mitochondrial conditions including FA.

We thank the FDA and the Advisory Committee for their commitment to including the patient perspective in regulatory decision making. We appreciate the opportunity to support the Barth syndrome community as we have heard from them directly how they believe the benefits outweigh the risks when considering elamipretide as a treatment.

Thank you for considering our comments. Please do not hesitate to contact FARA if you have any questions for us or if there is any way in which we might be helpful.

Sincerely,



Jennifer Farmer, MS Chief
Executive Officer

MitoAction
Peer Organization

T 888.648.6228 E info@mitoaction.org PO Box 310 Novi, MI. 48376 www.mitoaction.org

September 25, 2024

Submission to docket FDA-2024-N-3969

Dear Esteemed Members of the FDA Advisory Committee,

On behalf of MitoAction, I am writing to express our strong support for the approval of elamipretide as a treatment for Barth syndrome. Today, there is no FDA-approved treatment for this ultra-rare disease.

MitoAction is a nonprofit organization founded in 2005 by patients, parents, and healthcare leaders, with the mission to improve the quality of life for children, adults, and families living with mitochondrial disease. Over the years, we have expanded into a transformative and impactful community, supporting thousands of patients and families through education, advocacy, and engagement with the scientific and pharmaceutical communities to advance much-needed research and therapies.

Because mitochondria are responsible for turning nutrients into energy, the effects of Barth syndrome are profound, leading to debilitating symptoms such as heart failure, muscle weakness, chronic fatigue, and growth delays. As of 2022, there is no FDA-approved therapy available for this disease, leaving patients and families without viable treatment options to manage this devastating condition.

For the approximately 1 in 300,000 to 400,000 people affected by Barth syndrome in the United States, elamipretide represents a significant opportunity. Elamipretide is uniquely positioned to address the mitochondrial dysfunction at the heart of Barth syndrome by supporting and stabilizing cardiolipin and improving energy production at the cellular level. Clinical trials have demonstrated that elamipretide holds potential in improving mitochondrial energy output, helping to alleviate symptoms like muscle weakness and fatigue—core challenges for patients with Barth syndrome. For a condition where every patient is biochemically distinct, this treatment could offer meaningful, personalized benefits.

Families affected by Barth syndrome face tremendous uncertainty, as even minor stresses—such as illness, poor nutrition, or fatigue—can exacerbate the condition and lead to rapid deterioration of health. With such high stakes, the availability of a targeted therapy like elamipretide could provide patients with greater stability and resilience in managing their symptoms. Physicians who specialize in mitochondrial diseases understand that no two patients respond the same way to treatment. Therefore, having an option like elamipretide, which addresses the underlying mitochondrial dysfunction, would be a vital tool in the individualized care for those with Barth syndrome.

At MitoAction, we hear from patients and caregivers every day who are grappling with the daily hardships caused by mitochondrial diseases. Many of those with Barth syndrome are unable to participate in activities that most of us take for granted due to severe energy deficits. The

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approval of elamipretide would mark a critical turning point for these patients and their families, providing not only physical improvements but also emotional relief, knowing that they finally have access to a therapy that could improve their quality of life.

We urge you to consider the profound impact that elamipretide could have on the mitochondrial disease community, and specifically for patients living with Barth syndrome. The unmet medical need in this population is substantial, and elamipretide offers the first real hope for a therapy that addresses the core dysfunction of their disease. Its approval would represent a monumental step forward, offering these patients and their families a path toward better health outcomes and a more hopeful future.

Thank you for your attention to this critical matter. We remain dedicated to advocating for those affected by mitochondrial diseases and are available to support your efforts as you consider the approval of elamipretide. We believe this therapy has the potential to truly change lives and look forward to a positive outcome for the thousands of families who are depending on it.

Sincerely,

Kira Mann
Chief Executive Officer, MitoAction

THE POLG FOUNDATION

PoL G Foundation (Brian Tseng)

Peer Organization

September 26, 2024 Submission to Docket FDA -2024-N-3969
Dear Members of the FDA Advisory Committee,

I am writing on behalf of the POLG Foundation (TPF) and the many affected patients, families, clinicians, and researchers we represent. We urge you to thoroughly review the evidence package for elamipretide and support its approval as an essential treatment for individuals living with Barth syndrome, an ultra-rare mitochondrial disease.

Mitochondrial diseases are a collection of rare genetic disorders that cause the electron transport chain in mitochondria to not function properly. For people living with mitochondrial disease, this can lead to profound and life-altering “powering-down” issues, including muscle weakness, heart dysfunction, neurological deficits, and organ failure. These conditions can be fatal, especially in ultra-rare disorders like Barth syndrome.

As of today, there are no FDA-approved therapies for any mitochondrial diseases. This highlights the extreme unmet medical need in our community. Elamipretide has shown promise in addressing the underlying mitochondrial dysfunction specific to Barth syndrome. This is crucial for the Barth syndrome community as improved muscle strength, cardiac function, and overall energy production offers meaningful benefit for patients and families.

Your careful consideration of the available evidence and favorable recommendation will make a monumental difference in the lives of these individuals. While mitochondrial diseases are rare, the human impact is vast. All patients living with mitochondrial disorders deserve the chance to benefit from modern medical advances, and the Barth syndrome community is no exception.

On behalf of TPF, I respectfully ask you to support the approval of elamipretide for use in Barth syndrome. Your positive consideration will bring hope to families facing these devastating diseases, ensuring that Barth syndrome patients have a therapeutic option in their battle against mitochondrial dysfunction.

Sincerely,

Brian Tseng MD/PhD

Brian Tseng MD/PhD
Chief Scientific Officer
The PolG Foundation

UMDF
Peer Organization

September 25, 2024
Submission to docket FDA-2024-N-3969

Dear Members of the FDA Advisory Committee,

I am writing on behalf of the United Mitochondrial Disease Foundation (UMDF), our board of trustees, and the many affected patients, families, clinicians, and researchers we represent. We urge you to thoughtfully and thoroughly review the evidence for elamipretide and support its approval as an essential treatment for individuals living with Barth syndrome, an ultra-rare mitochondrial disease.

Mitochondrial diseases are a collection of rare genetic disorders that cause the electron transport chain in mitochondria to not function properly. For people living with mitochondrial disease, this can lead to profound and life-altering symptoms, including muscle weakness, heart dysfunction, neurological deficits, and organ failure. These conditions can be fatal, especially in ultra-rare disorders like Barth syndrome, which presents unique clinical challenges.

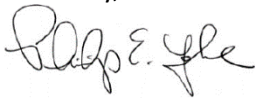
As of today, there are no FDA-approved therapies for mitochondrial diseases. This highlights the extreme unmet medical need in our community. We ask you to consider the child whose heart gives out from cardiomyopathy, the adult who can no longer walk or breathe unaided, and the parents who spend sleepless nights fearing for their child's future. These patients deserve access to every possible therapeutic option, including innovative treatments that could offer improved quality of life and extended survival.

Elamipretide has shown promise in addressing the underlying mitochondrial dysfunction specific to Barth syndrome. This is crucial for the Barth syndrome community, where nuanced biological and clinical factors make targeted treatments a lifeline. The potential for therapies to improve muscle strength, cardiac function, and overall energy production in patients with Barth syndrome offers renewed hope for patients and families.

Your consideration of the available evidence and favorable recommendation will make a monumental difference in the lives of these individuals. While mitochondrial diseases are rare, the human impact is vast. All patients living with mitochondrial disorders deserve the chance to benefit from modern medical advances, and the Barth syndrome community is no exception.

On behalf of UMDF, I respectfully ask you to support the approval of elamipretide for use in Barth syndrome. Your careful review and decision will bring hope to families facing these devastating diseases, ensuring that Barth syndrome patients have a therapeutic option in their battle against mitochondrial dysfunction.

Sincerely,



Dr. Philip Yeske, United Mitochondrial Disease foundation, Interim Managing Director & Alliance Officer

UMDF Patient Advisory Council
Peer Organization

Submission to docket FDA-2024-N-3969

Dear Members of the FDA Advisory Committee,

We, the undersigned members of the Patient Advisory Council of the United Mitochondrial Disease Foundation, write today to urge your thoughtful consideration and approval of elamipretide as a therapy for the rare mitochondrial disease Barth syndrome. As caregivers to mitochondrial disease patients – or patients ourselves, we each know firsthand the devastating impact of this disease. We have seen the consequences of how diseases like Barth Syndrome wreak havoc on the parts of the body that need the most energy like the heart, brain, and muscles. Amplifying the tragedy is the failure of any mitochondrial disease treatment thus far to meet FDA approval. Today, you have the power to help that change. When you make your recommendation, think of us who have had to stand by as this disease slowly takes away the ability to walk, talk, eat, and breathe -- and far too frequently, takes life itself. This community deserves access to any therapy proven safe that could improve function and perhaps even extend lives. We believe all evidence shows that for Barth syndrome, elamipretide fits this description. Patients have reported greater energy levels, muscle strength, and improved heart health. Your actions today could truly mean the difference between life and death for these families. With a positive recommendation, you can take the first step in turning the tide against mitochondrial disease and give a chance to families like ours who otherwise face a bleak outlook. Thank you for your consideration.

Sincerely,

Jaclyn Leit, UMDF Patient Advisory Council (PAC) Chair
Paul Lore, UMDF PAC Member
Ann Korsen, UMDF PAC Member
Jenny Hobbs, UMDF PAC Member
Katy Neveu, UMDF PAC Member
Nikki Huggan, UMDF PAC Member
Aneesa Licorish, UMDF PAC Member
Christina Satcher, UMDF PAC Member
Nick Stancombe, UMDF PAC Member
Grace Robinson, UMDF PAC Member
Joy Krumdiack, UMDF PAC Member