

Stronger Together

#StrongerTogether was our theme for the 2022 International Barth Syndrome Scientific, Medical, and Family Conference. COVID-19 dampened our ambitions to come together in Florida for the Conference, yet we continue to believe that We Are #StrongerTogether.

Instead, BSF's "Stronger Together World Tour" (#STWT) is expanding the critical lifeline of the BSF community through regional events that are geographically accessible in these challenging times. Barth families, researchers, and healthcare providers unite in strategic locations across the world for our common cause: to build and strengthen relationships through a shared experience of education, research, and camaraderie. The full brochure begins on page 2, detailing the dates and agendas for each stop in the US, as well as information on events outside of the US.

In addition to STWT, we convened our second Scientific and Medical Virtual Symposium, July 20-22, 2022. Our research community continues to make strides in advancing Barth

syndrome science and medicine. Over 170 attendees joined 16 presenters in discussing:

- Barth Syndrome Cardiomyopathy: Challenges & Opportunities
- Treatment & Quality of Life for Barth Syndrome
- Barth Syndrome Biology
- Barth Syndrome in Physiology
- Cardioliipin in Physiology

We've included the full symposium program in this issue, detailing the presentation topics and speaker bios. Recordings of the presentations, including Q&A are available on BSF's website at www.barthsyndrome.org.

While we are disappointed that we cannot gather as we have in previously at our international conferences, we are committed to doing everything we can to maintain our community bonds during these still uncertain times. Most importantly, we will never, ever give up and are planning to gather again as a global community in 2024!

In This Issue

STWT World Tour	P. 2	Gene Therapy	P. 21	Neutropenia Series	P. 26
Community Spotlight	P. 5	Advocacy In Action	P. 22	Community Crossword	P. 27
Symposium	P. 6	Rare Policy Summit	P. 24		
Research Strategy	P. 15	FDA Workshop	P. 25		



COMMITMENT TO OUR VISION

We continue to believe that we are #StrongerTogether, so we are hitting the road to be #StrongerTogether in regional gatherings around the globe!

THE #STRONGERTOGETHER WORLD TOUR (#STWT)

Our mission is "Saving lives through education, advances in treatments and finding a cure for Barth syndrome." COVID-19 has not only changed the world, but it has caused us to think creatively about new ways we can achieve our mission. BSF's "Stronger Together World Tour" (#STWT) was designed to expand the critical lifeline of the BSF community through regional events that are geographically accessible in these challenging times. Barth families, researchers, and healthcare providers will unite in strategic locations across the world for our common cause: to build and strengthen relationships through a shared experience of education, research, and camaraderie. We educate healthcare providers and families to learn new ways in which research and clinical advancements have the potential to allow those with Barth syndrome to live longer and fuller lives. We deepen researchers' resolve to end this dreadful disease by introducing them to the people who will benefit from their discoveries. And we are creating opportunities to fortify the relationships between families so they can support each other across the journey of living with or caring for someone with Barth syndrome.

TOUR-STOP AGENDA

Day 1

Community members arrive at the venue in the afternoon
BSF-sponsored casual dinner at venue with social opportunities

Day 2

BSF-sponsored breakfast, lunch and dinner
Barth syndrome educational sessions
Research updates
Registry participation
Afternoon activities

Day 3

BSF-sponsored breakfast

U.S. STOPS

- Fitchburg, Massachusetts (Great Wolf Lodge) Fri, Jul 8 - Sun, Jul 10, 2022
- Gurnee, Illinois (Great Wolf Lodge) Sun, Jul 24 - Tue, Jul 26, 2022
- LaGrange, Georgia (Great Wolf Lodge) Fri, Oct 7 - Sun, Oct 9, 2022
- Scottsdale, Arizona (Great Wolf Lodge) Fri, Oct 21 - Sun, Oct 23, 2022

LIVE OUTSIDE OF THE U.S.?

Reach out to a local BSF affiliate or regional ambassador to learn more about opportunities in your area.

- Calgary, Canada (Fri, Aug 19 – Sun, Aug 21, 2022)
Contact Susan Hone (shone@barthsyndrome.ca)
- Helvoirt, The Netherlands (Sat, Sep, 10, 2022)
Contact Peter van Loo (peter.vanloo@barthstrong.org)
- Leicester, England (Sat, Oct 1 – Sun, Oct 2, 2022)
Contact Michaela Damin (michaela.damin@barthsyndrome.org.uk)
- Paris, France (Sat, Dec 10 - Sun, Dec 11, 2022)
Contact Florence Mannes (florence@barthfrance.org)

TRAVEL AND LODGING ASSISTANCE

Want to attend #STWT but finances are tight? You may be eligible for the National Organization for Rare Disorders (NORD), Rare Disease Educational Support Program. These funds are subject to availability. So, don't wait to apply. For more information contact rdeducate@rarediseases.org or 860.556.2208.

Help Support The Stronger Together World Tour!

Now more than ever, Barth kids and adults need joy in their lives.



BSF has partnered with Great Wolf Lodge to give Barth families a special, memorable experience doing what so many in our community love: pool time with Barth friends!



You can give Barth families the gift of JOY by making a donation to support the Stronger Together World Tour. Your generosity puts smiles on peoples' faces, as they make and build memories and connections which will last for years to come.

YOUR DOLLARS CAN DRIVE CHANGE!
Email Emily Milligan at emily.milligan@barthsyndrome.org or a local BSF affiliate to help make #STWT a global reality through your financial support. make your gift today!

Community Spotlight: Meet Zoé



Like the falling leaves in September each year, many Barth parents visit their sons' teachers and peers to explain what it is like to live with Barth syndrome. BSF Board Member, Florence Mannes, is one of those parents. However, as her son, Raphaël, got older, he expressed interest in explaining Barth syndrome himself to his peers, but he wanted some support. Around the same time, some French families approached Florence, asking to help them explain Barth syndrome to family members, care takers, and others. "That's how the idea of the booklet was born," Florence explained. She went to work drafting the booklet, which ultimately was published in two volumes: "Barth Syndrome: A Little Book for Children" and "Barth Syndrome: A Little Book for Teenagers."

Early in the process, Florence reached out to longtime friend, Zoé Viot, an accomplished illustrator. "I was raised with Zoé; all of her drawings are part of my childhood. She created our wedding invitation," said, Florence. "She knows what living with a special needs

child means, and I was convinced she would be able to create a booklet both informative and fun...she did more than that, and the result was better than we expected."

Zoé always loved to draw and went on to train in graphic arts. "At the end of my studies, I spent two years in communication agencies as an artistic director, but I finally chose to become an illustrator to have more freedom; And it's been going on for 20 years!" Zoé said of her career in the arts.

Zoé's 18-year-old daughter has multiple disabilities including autism. Zoe used her talents to share her family's daily life in an illustrated blog to "de-dramatize" the life of a caregiver. "I like to use slightly caustic humor in order to distance our story from those of pity or inspiration that generally accompany conversations around disability," Zoé said. She first learned about Barth syndrome from Florence, whose son was born some years after her daughter.

When Florence approached Zoé to illustrate the book, she immediately agreed. "Illustrations help capture the audience's attention and get the message across more effectively than words alone, especially in today's world where you only have a few seconds to hold the reader's or viewer's attention," Zoé explained.

The booklets explain Barth syndrome in an accessible and engaging format. They also open the conversation around access and inclusion for people with disabilities, moving away from the common narrative of "pity" and "less than" that stigmatizes disability. Both booklets are available as free downloadable PDFs on the BSF website at www.barthsyndrome.org. Thank you to Florence and Zoé for creating these valuable resources!

You can find out more about Zoé's work via her website at: www.zoe-illustratrice.com



2022 International Scientific and Medical Virtual Symposium July 20-22, 2022



Agenda

July 20, 2022

11:30AM ET (17:30 CET) - 1:00PM ET (19:00 CET)

Barth Syndrome Cardiomyopathy: Challenges & Opportunities

Extended recovery of cardiac function after severe infantile cardiomyopathy presentation in Barth syndrome

Jessie Yester, UPMC Children's Hospital of Pittsburgh

Longitudinal observational study of cardiac outcome risk factor prediction in children, adolescents, and adults with Barth syndrome

Carolyn Taylor, Medical University of South Carolina

The Barth Syndrome Arrhythmia Project

Colin Phoon & Reina Tan, NYU Langone Health

July 21, 2022

11:30AM ET (17:30 CET) - 1:00PM ET (19:00 CET)

Treatment & Quality of Life for Barth Syndrome

Qualitative and quantitative measure of fatigue in Barth syndrome

Stacey Reynolds, Virginia Commonwealth University

Quality of life in Barth syndrome

Brittany Hornby, Kennedy Krieger Institute

Long-term efficacy and safety of elamipretide in patients with Barth syndrome: open label extension results of TAZPOWER through 168 weeks

Jim Carr, Stealth BioTherapeutics

1:30PM ET (19:30 CET) - 3:00PM ET (21:00 CET)

Barth Syndrome Biology

Barth syndrome's unsung phenotype: 3-methylglutaconic aciduria

Elizabeth A. Jennings, University of Nevada, Reno

Engineered isoforms of Tafazzin: activity, stability, and potential therapeutic utility

Michael T. Chin, Tufts Medical Center

Advances in understanding cardiolipin synthesis and pathological effects of dysregulation in cells and animals

Robin E. Duncan, University of Waterloo

July 22, 2022

11:30AM ET (17:30 CET) - 1:00PM ET (19:00 CET)

Barth Syndrome in Physiology

Genomewide association study in a mouse model of Barth syndrome

Suya Wang, Boston Children's Hospital

Activation of stress response signaling rewires cardiac metabolism in Barth syndrome

Jan Dudek, University of Würzburg

The molecular composition of cardiolipins is tightly coupled with the nutritional lipid environment

Markus A. Keller, Medical University of Innsbruck

1:00PM ET (19:00 CET) - 1:30PM ET (19:30 CET)

Strategic Partnerships with Barth Syndrome Foundation

Please join Erik Lontok, BSF's Director of Research, for a lunchtime conversation of the initiatives, efforts, and collaborations driving the Foundation's R&D Program

1:30PM ET (19:30 CET) - 3:00PM ET (21:00 CET)

Cardiolipin in Physiology

Cardiolipin coordinates lipopolysaccharide-induced respiratory Complex II disassembly & degradation

Mack B. Reynolds, University of Michigan Medical School

Cardiolipin bound to mitochondrial ADP/ATP carrier supports the structure and transport-related function

Nanami Senoo, Johns Hopkins University School of Medicine

Cardiolipin metabolism regulates myoD1 expression and muscle development

Linh Vo, Wayne State University

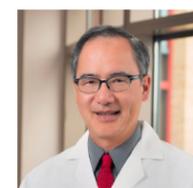


Presenters



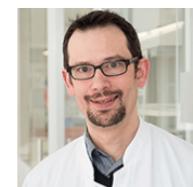
Jim Carr, Stealth BioTherapeutics

Jim Carr is the Chief Clinical Development Officer of Stealth BioTherapeutics. He brings over 20 years of industry experience in the areas of clinical development, medical affairs, lifecycle management, new product planning, and global marketing to Stealth. Previously, Jim was an Executive Director in the Global Cardiovascular Franchise at GlaxoSmithKline. Prior to GlaxoSmithKline, he held the role of Vice President of Clinical Development at Arca Biopharma. Jim's educational background is a Doctor of Pharmacy degree from the University of Minnesota and post-graduate training in clinical cardiovascular pharmacology. Prior to joining the pharmaceutical industry, he was on the clinical faculty at the University at Buffalo-SUNY School of Pharmacy.



Michael T. Chin, Tufts Medical Center

Dr. Chin is a Professor of Medicine at Tufts University School of Medicine, the Director of the Medical Scientist Training Program and the Research Director for the Tufts Hypertrophic Cardiomyopathy Center. His research interests include studying the molecular mechanisms of heart failure with a particular interest in genetic cardiomyopathies. His current research is focused on the development of an enzyme replacement therapy for Barth Syndrome, a rare inherited disorder of mitochondria. He also oversees a translational research program dedicated to multi-omic analyses of tissue from patients with Hypertrophic Cardiomyopathy and studying pathogenic mechanisms in mouse models.



Jan Dudek, University of Würzburg

Jan Dudek completed his PhD in 2006 in the Department of Biochemistry and Molecular Biology at the University of Freiburg, where he studied mitochondrial protein translocases involved in the transport of newly synthesized proteins into the mitochondria. Between 2007 and 2010, he joined a collaborative project at the Beatson Institute for Cancer Research, Glasgow, UK and at the University of California at San Francisco (UCSF), USA working on oncogenic signaling pathways. In 2010 he joined the Department of Cellular Biochemistry at the University of Göttingen as a project leader, studying the structural and functional defects of the mitochondrial respiratory chain in human diseases. In 2018 he started his junior research group at the Comprehensive Heart Failure Center elucidating the role of mitochondrial dysfunction in cardiomyopathies.



Robin E. Duncan, University of Waterloo

Professor Duncan is an Associate Professor in the Faculty of Health Sciences at the University of Waterloo. She completed her BSc (Hons) at the University of Guelph (Biological Sciences), followed by a PhD at the University of Toronto (Nutritional Sciences), and a Postdoctoral Fellowship at the University of California, Berkeley (Nutritional Science and Toxicology). Her laboratory is focused on the identification of novel enzymes in lipid metabolism, and the study of bioactive lipids in physiological and pathophysiological processes. This work includes both understanding how endogenous lipids function in cellular processes and signaling, and how exogenous bioactive lipids may function therapeutically. Dr. Duncan is the recipient

of an Early Researcher Award (Government of Ontario), an Early Career Investigator Award (Canadian Lipoprotein Conference), a Distinguished Teacher Award (University of Waterloo), and a Discovery Accelerator Supplement Award from the Natural Sciences and Engineering Research Council of Canada (NSERC). She is an Academic Editor for PLoS ONE, and a member of the editorial boards for Molecular and Cellular Biochemistry and Molecular Nutrition and Food Research, and serves on grant panels for the Heart and Stroke Foundation of Canada and Diabetes Canada. Her work has been funded by grants from NSERC, Diabetes Canada, the Canada Foundation for Innovation, and the Barth Syndrome Foundation (International and Canadian).



Brittany Hornby, Kennedy Krieger Institute

Brittany Hornby is a senior physical therapist in the Outpatient Physical Therapy Department at Kennedy Krieger Institute. She received a Bachelor of Science degree from James Madison University. She received her Doctorate of Physical Therapy from George Washington University. She serves as Adjunct Assistant Professor for the Department of Health, Human Function and Rehabilitation Services at the George Washington University School of Medicine and Health Sciences and the Department of Physical Therapy and Rehabilitation Science at the University of Maryland School of Medicine. Her current research interests include functional ability and quality of life in patients with Barth syndrome.



Elizabeth A. Jennings, University of Nevada, Reno

Elizabeth Jennings completed her undergraduate education at the University of Nevada, Reno where she earned two Bachelor's degrees in Nutritional Sciences/Dietetics and Biology with a minor in Biochemistry. She recently completed her second year in the UNR Molecular Biosciences Graduate Program where she is pursuing a PhD in Biochemistry. She has a passion for teaching and has served as a TA for a Molecular Biology Laboratory course for two years. Elizabeth is completing her graduate research in Dr. Robert O. Ryan's laboratory which studies secondary 3-methylglutaconic aciduria, a phenotypic feature of numerous inborn errors of metabolism including Barth syndrome.



Markus A. Keller, Medical University of Innsbruck

Markus Keller is a trained Chemist who started studying lipid metabolism in the context of biomedical research during his PhD. The focus of his scientific work lies in the enzymology and properties of the lipid metabolic network. He applies LC-MS/MS based approaches and bioinformatical strategies to elucidate the pathomechanisms of inborn errors in lipid metabolism.



Colin Phoon, NYU Langone Health

Dr. Phoon is an Associate Professor of Pediatrics (Cardiology), at New York University Langone Health and Grossman School of Medicine, Division of Pediatric Cardiology, Department of Pediatrics. He is investigating the role of mitochondria and cardiolipin in the pathogenesis of cardiomyopathy and Barth syndrome, with a focus on mouse models to investigate both cellular mechanisms and potential therapeutic targets. He has been involved in Barth syndrome research in a close collaboration with Drs. Michael Schlame and Mindong Ren for over a dozen years. As a principal investigator or co-investigator on several projects relevant to a broad spectrum of cardiovascular disease in

small animal models, he is especially interested in heart development and heart imaging. Dr. Phoon is a pediatric cardiologist at New York University Grossman School of Medicine, where he has worked since completing his training in 1996.



Stacey Reynolds, Virginia Commonwealth University

Dr. Stacey Reynolds is a Professor and Director of Research in the Department of Occupational Therapy at Virginia Commonwealth University (VCU). At VCU she directs the Sensory Processing and Stress Evaluation (SPASE) Lab where her aim is to discover neurological mechanisms underlying sensory-motor deficits in children and develop innovative treatments. She has worked with the Barth syndrome community for over a decade examining sensory and motor features that impact feeding, eating, and swallowing. Her more recent work with the Barth community focuses on the relationship between activity levels, sleep, and fatigue and the relationship of these variables with nutrition.



Mack B. Reynolds, University of Michigan Medical School

Mack graduated from the University of California at Davis in 2017 with a B.S. in biochemistry. At UC Davis, he worked as an undergraduate researcher in Dr. Scott Simon's lab studying innate immune cell trafficking in a mouse model of Staphylococcus aureus skin and soft tissue infection. Following graduation, Mack worked in the same lab developing a microfluidic device to predict susceptibility to atherosclerosis in a clinical setting. Mack is now a Ph.D. student in the Program in Immunology at the University of Michigan working in the lab of Dr. Mary O'Riordan.



Nanami Senoo, Johns Hopkins University

Nanami is a postdoctoral fellow in Johns Hopkins University Department of Physiology with research focuses on phospholipid biology and mitochondrial energy metabolism, currently holding the American Heart Association Postdoctoral Fellowship cofounded with Barth Syndrome Foundation. She received her PhD in Food and Nutritional Science, University of Shizuoka, Japan.



Reina Tan, NYU Langone Health

Dr. Tan is investigating the incidence of arrhythmias in Barth Syndrome patients. She is the co-Principal Investigator with Dr. Colin Phoon on the project, "Collaborative Registry to Determine the Natural History of Barth Syndrome." She is a pediatric cardiologist and pediatric electrophysiologist at New York University school of medicine – Hassenfeld Children's Hospital. She co-chairs the research committee in the division of pediatric cardiology. Dr. Tan is board certified in pediatrics, pediatric cardiology and pediatric electrophysiology.



Carolyn Taylor, Medical University of South Carolina

Dr. Taylor is a pediatric cardiologist with additional specialty training as a pediatric echocardiographer. Her research and clinical interests are in the areas of imaging and evaluation of cardiac function. Assessment of cardiac performance using echocardiography as well as evaluation of functional capacity in various forms of cardiomyopathy and cardio-skeletal myopathy are central to her clinical practice and research

effort. She has been actively involved in the Barth syndrome scientific and research community since the early 2000s, and has authored and co-authored publications on cardiomyopathy and exercise capacity (through collaborations with Todd Cade), and conducted research utilizing on-site studies at the BSF conference and findings from the Barth Syndrome Registry.



Linh Vo, Wayne State University

Linh Vo is currently a Graduate Research Assistant in Dr. Miriam Greenberg's lab at Wayne State University. Her research project aims to elucidate the mechanisms underlying skeletal myopathy in Barth syndrome, a rare metabolic disease caused by abnormalities in the mitochondrial phospholipid cardiolipin. She believes that research and science are keys to a future with no Barth syndrome. Linh Vo holds a Master's degree in Medical Sciences from University of Tsukuba. She also holds a Bachelor's degree from University of Science – VNUHCM in Biotechnology.



Suya Wang, Boston Children's Hospital

Dr. Suya Wang is postdoctoral researcher in Dr. William Pu's laboratory at Boston's Children's Hospital. As an undergrad, she majored in Pharmacology at China Pharmaceutical University and was fascinated by how therapeutic agents change people's life. Dr. Wang later earned her PhD in Pharmacology and Toxicology from University of Kansas, where she started her journey exploring cardiac diseases. As a pharmacologist and biologist, Dr. Wang is interested in developing and optimizing novel therapeutic approaches to genetic disorders. To her, bio-medicine should not be just a research paper but a product that is safe, translatable and achievable in clinical practice.



Jessie Yester, Nationwide Children's Hospital

Jessie Yester completed her undergraduate education at North Carolina State University and her MD, PhD at Virginia Commonwealth University. She completed her Pediatric Cardiology Fellowship at UMPC Children's Hospital of Pittsburgh and Clinical Fellowship in Pediatric Heart Failure, Cardiomyopathy, and Transplantation at the Texas Children's Hospital. This fall, she will start as faculty at the Nationwide Children's Hospital. Her research interests include cardiotoxicity and determining the molecular pathways of cardiomyocyte proliferation and regeneration.

Community Presenter



John Wilkins

Opening Comments for *Treatment and Quality of Life for Barth Syndrome*

As a longtime member of the community and an individual affected by Barth syndrome, Mr. John Wilkins brings a unique vantage point to the issues facing the BSF. Volunteering in every capacity, John has participated in numerous committees and research studies, as well as having served on the BSF Board of Directors. Mr. Wilkins earned an A.S. in Computer Information Technology from Southeast Community College in Lincoln, Nebraska, and works part time as a computer consultant. John lives in Lincoln, Nebraska

Session Chairs



Steven Claypool, Johns Hopkins University
Chair for *Cardiolipin in Physiology*

Dr. Steven Michael Claypool is an assistant professor of physiology at the Johns Hopkins University School of Medicine. His research focuses on mitochondrial lipid metabolism and the contribution of phospholipids in mitochondrial function and dysfunction. Dr. Claypool received his B.A. in biological sciences and his M.A. in molecular, cellular and developmental biology from the University of California, Santa Barbara. He earned a Ph.D. in immunology from Harvard University and performed a postdoctoral fellowship in mitochondrial biology at University of California, Los Angeles. He has authored or co-authored several peer-reviewed publications, and has presented his work extensively.



Miriam Greenberg, Wayne State University
Chair for *Barth Syndrome Cardiomyopathy*

Dr. Greenberg is a Professor of Biological Sciences at Wayne State University in Detroit, MI. She is an expert on phospholipid metabolism and brings a wealth of knowledge about cardiolipin in yeast and mammalian cells that has and will continue to advance scientific knowledge about some of the underlying biochemical issues in Barth syndrome.



Grant Hatch, University of Manitoba
Chair for *Barth Syndrome Biology*

Dr. Hatch's research interests focus on metabolism and pharmacological modulation of phospholipids (including cardiolipin) in the mammalian heart and cells in culture. He has published numerous papers on these topics.



Riekelt Houtkooper, AMC University of Amsterdam
Chair for *Barth Syndrome in Physiology*

Dr. Riekelt H. Houtkooper received his PhD degree from the laboratory Genetic Metabolic Diseases of the Academic Medical Center Amsterdam (NL), working under supervision of Prof. Ronald Wanders and Dr. Frédéric Vaz. His research centered on cardiolipin metabolism, particularly in relation to the rare mitochondrial disorder Barth syndrome. Riekelt joined the lab of prof. Johan Auwerx at EPFL Lausanne (Switzerland) for a postdoctoral project geared towards understanding and treating more common metabolic diseases. During these years, he became interested in the metabolic aspects of aging. Early 2012 Riekelt moved back to Amsterdam to start his own group, for which he received funding from NWO and the ERC. Current research in the group focuses on molecular and translational metabolism, both in the context of inborn errors of metabolism and aging.



Erik Lontok, Director of Research, Barth Syndrome Foundation

Erik Lontok graduated with a PhD in Biochemistry from the University of California, San Francisco, and upon moving to the Maryland area, served as an Adjunct Professor of Biochemistry for the University of Maryland, College Park. As Director of Research, Erik is responsible for the Foundation's research grantmaking and contracts, while also serving as the scientific ambassador for BSF, facilitating collaborations amongst Barth syndrome researchers and external partners. Erik's passion is to engage, learn, and apply knowledge to advance disease research, with the ultimate goal of effective treatments for affected individuals.



Hilary Vernon, Johns Hopkins University and at the Kennedy Krieger Institute Chair for *Treatment and Quality of Life for Barth Syndrome*

Dr. Vernon's research interests include understanding intermediary metabolism in Barth syndrome and in disorders of branch chain amino acid metabolism. Dr. Vernon is the director of the Mitochondrial Medicine Center at Johns Hopkins Hospital and the Barth Syndrome Interdisciplinary Clinic at the Kennedy Krieger Institute. She is also the co-director of the Department of Genetic Medicine Clinical Trials Unit at Johns Hopkins University School of Medicine. Dr. Vernon received her MD and PhD from Rutgers University, New Brunswick, NJ, USA. She completed residencies in Genetics and Pediatrics at Johns Hopkins University, and a fellowship in Clinical Laboratory Biochemical Genetics at Johns Hopkins University. She is board certified in Pediatrics, Clinical Genetics, and Clinical Laboratory Biochemical Genetics.

Watch recordings of all symposium presentations, including Q&As, at: www.barthsyndrome.org/symposium



Help Support BSF

Since 2000, BSF has been a lifeline for those who suffer from Barth syndrome, offering 24/7 support, pioneering standards of care and diagnosis, creating collaborations between clinicians, researchers and patients, and most importantly, making sure no person with Barth syndrome is ever alone.

Your support is vital to the success of our mission, so please consider making a gift today.

Donate at www.barthsyndrome.org/donate



BSF's Research Strategy

Since the launch of our peer-reviewed grant program in 2002, we have supported research projects that span discovery science, physiological and psychosocial characterization our community, to innovative cellular and animal models of disease. As Barth syndrome science has matured, so too has our approach.

Announced in 2021, our new Strategic Plan includes an expansion of Research alongside Development efforts to get to safe therapies faster for our community of Barth syndrome-affected individuals and families.

With an R&D portfolio that spans Barth discovery and translational science, to clinical studies and trials, BSF aims to partner across sectors including academia, industry, government, and peer organizations to develop life-changing therapies and lessen the suffering caused by Barth syndrome.

As a non-profit partner, we invest in the research talent and scientific innovation required to de-risk potential therapeutic advancements for our community.

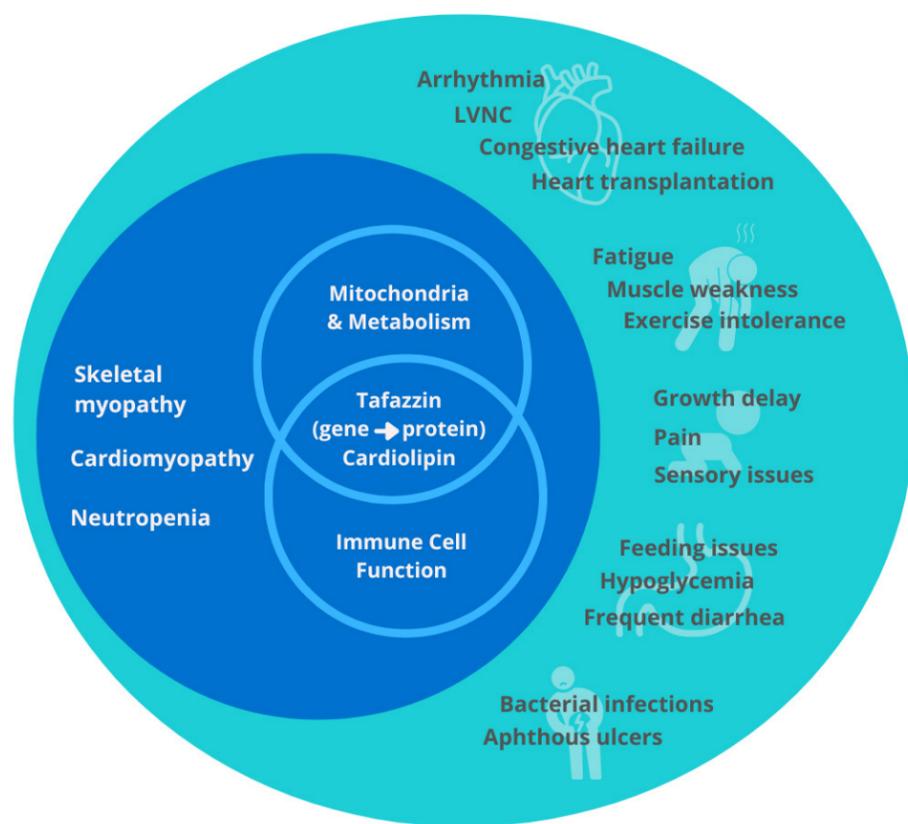
HOW WE MAKE R&D FUNDING DECISIONS

BSF follows a peer-review process for grant applications and research programs. The BSF Scientific and Medical Advisory Board as well as external reviewers are integral to the review process, with decisions around research tool development and consultant support employing a diligence process. The BSF Board of Directors or Executive Committee render the final funding decision for all expenditures.

BSF takes confidentiality and intellectual property rights very seriously. All reviewers are bound by confidentiality agreements consistent with best practices.

HOW WE FUND

The funding mechanism for projects depends on the specifics of the work, stage of the research and aspects of the organization/team doing the work. Commonly, BSF contracts through non-negotiable grant agreements, particularly for discovery and pre-clinical work in academia. However, for targeted programs, we also fund using strategic research agreements or investment vehicles. Research tools are typically funded with provisions giving BSF oversight of the assets our valuable donor dollars are supporting.



UNDERSTANDING THE ETIOLOGY OF BARTH SYNDROME

Barth syndrome is characterized by a constellation of symptoms of varying severity, with much to be understood regarding its phenotypic variability and the biochemical pathways that contribute to the disease manifestation and progression. Our funded efforts have contributed to the body of knowledge surrounding Barth syndrome while guiding our therapeutic development efforts.

FOSTERING AN OPEN, INCLUSIVE, & COLLABORATIVE RESEARCH ENVIRONMENT

Robust, collaborative, replicable research is critical for faster progress. The Foundation works to build an open and collaborative research environment through strategic investment in:

- Productive and rigorous dialogue between affected individuals, families, and researchers
- Well-characterized and accessible research tools
- Sharing of biosamples and data – with appropriate data embargo periods to protect a researcher IP
- Open communication and collaboration among multidisciplinary researchers and experts

DEVELOPING IMPACTFUL THERAPIES FOR OUR COMMUNITY

BSF remains focused on developing life-changing therapies for individuals affected by Barth syndrome. Our current development opportunities include disease-modifying therapies that would address the underlying genetic basis of Barth syndrome or absence of enzymatic function by tafazzin, as well as identification and validation of novel or repurposed drugs. We further impact therapeutic development by working with industry on and advocating with regulators for study designs and clinical trial endpoints both tailored and achievable for an ultra-rare disease.

HOW WE ADVANCE RESEARCH & DEVELOPMENT

These programs span the scope of effort BSF employs to expeditiously reach our goal of safe and effective therapies for our community.

Seed Grants

The grant program is intentionally open-ended, calling for novel and iterative ideas across the spectrum of Barth syndrome research.

Follow-on Funding

We may issue add-on funding if a project shows significant progress and continued potential to improving our understanding of Barth syndrome or the development of promising treatments.

Targeted Priorities

Guided by collaborative discussions with clinical and subject-matter experts, these efforts aim to address key research gaps and unmet needs as reflected in BSF's Strategic Plan such as Barth Fatigue and Arrhythmias.

Consultant Support

As intellectual property advances through R&D, so do the requirements for research due diligence. BSF works with researchers to identify consultants who can advise teams on pre-IND enabling studies, regulatory data packages, and other specialized areas along critical path of therapeutic development.

Partnerships with Peer Organizations

Barth syndrome is a complex, multi-system disorder encompassing cardiac, mitochondrial, neuromuscular, gastrointestinal, metabolic, and immune pathologies. To leverage mission synergies, we actively seek opportunities to partner with disease organizations for the advancement of research as it overlaps with Barth syndrome pathophysiology and symptomology.

Expanding our Reach

These efforts have the potential to mutually advance our shared science while building interdisciplinary bridges to a broad field of trainees and young investigators.

RESOURCE-SHARING AND RESEARCH TOOLS

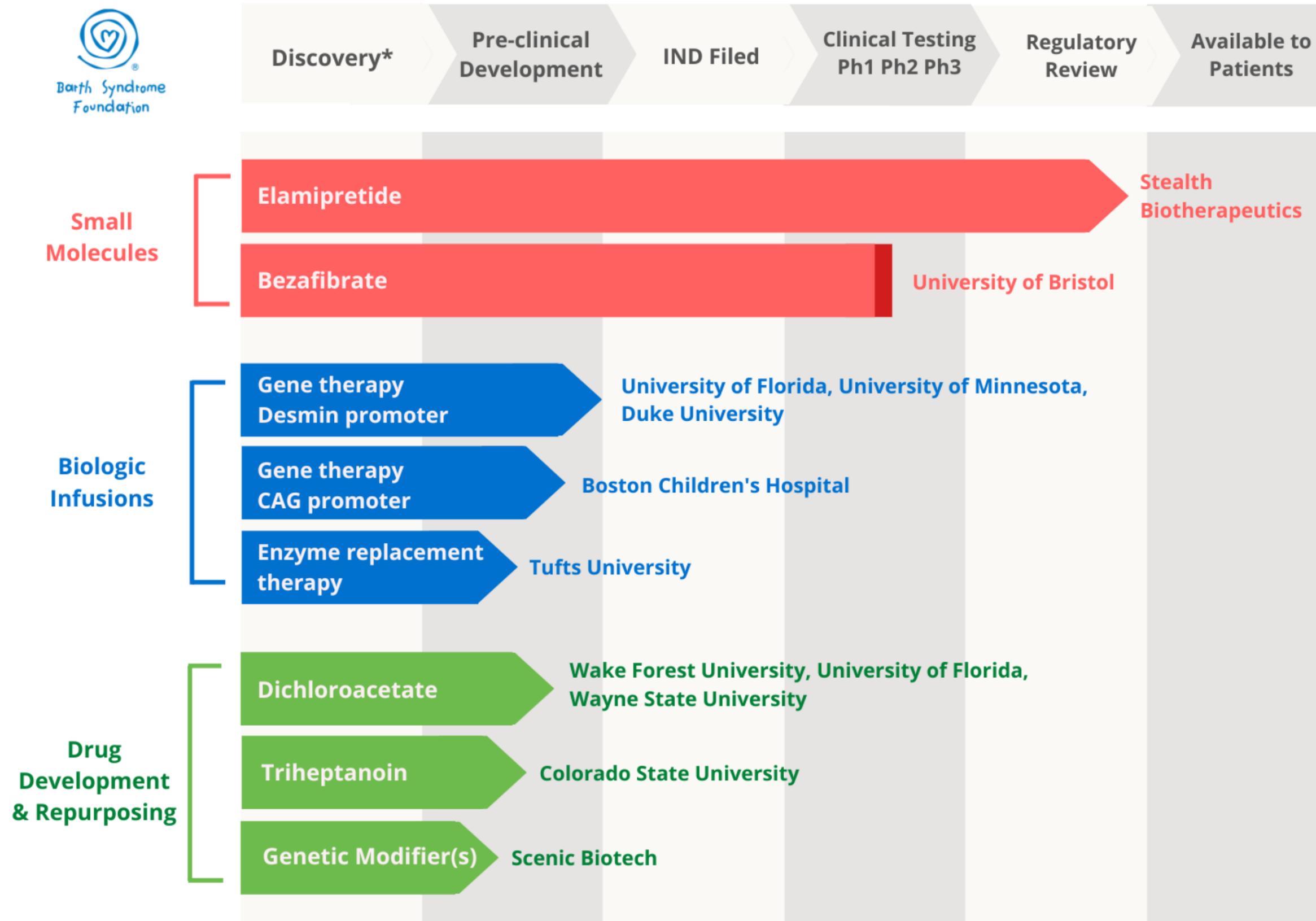
As technologies evolve, so do the tools researchers need to advance their work expeditiously and cost-effectively. We help to de-risk this aspect of R&D by creating and supporting non-competitive, accessible research assets including:

ResearchID, Patient Registry & Biorepository
 Diagnostic Technologies & Human Variants Database
 Cellular & Animal Models

To learn more and engage with the BSF R&D Program please email:

Erik.lontok@barthsyndrome.org – Director of Research
 Melissa.huang@barthsyndrome.org – Clinical Research Coordinator

Barth Syndrome R&D Pipeline



Bespoke Gene Therapy Consortium

Barth syndrome is one of 14 rare diseases invited to apply for the Accelerating Medicines Partnership® Bespoke Gene Therapy Consortium (AMP® BGTC).

The AMP®BGTC program is a public-private partnership between the National Institutes of Health (NIH), the U.S. Food and Drug Administration (FDA), multiple biopharmaceutical and life science companies, and non-profit and other organizations to transform the current model for developing new diagnostics and treatments.

Barth syndrome is a disease that happens because a single gene, TFAZZIN (aka TAZ), is impaired and not working-- a common situation in many rare diseases. This makes gene replacement therapy the ideal solution, by changing the one gene that is resulting in disease.

The NIH sees the potential for this therapy to address rare diseases caused by a single gene. "BSF has invested in Barth syndrome gene replacement therapy research since the early 2000s," said Erik Lontok, BSF's

Director of Research. "The BGTC invitation both validates our efforts and provides an immense opportunity for our community of affected individuals and their families, clinicians, and researchers who have been with us every step of the way."

The AMP®BGTC program is an opportunity to take a gene/disease all the way to a gene therapy clinical trial, with the five to six diseases that will be selected for the program, to be announced next year. According to an article published by the Regulatory Affairs Professionals Society (RAPS), "BGTC also plans to examine the current regulatory scheme for gene therapies and seek efficiencies that can speed development by streamlining the FDA approval process."

To find out more about the AMP®BGTC program, visit: <https://ncats.nih.gov/programs/BGTC>

BSF 2023 GRANT CYCLE IS OPEN!

BSF and our International Affiliates welcome innovative applications seeking grant funding to young and established investigators to generate the preliminary data required for successful follow-on funding available from major grant-making institutions such as the National Institutes of Health (NIH). Application Types:

Idea Award: US \$50,000 maximum Total Cost, 1-2 years in duration. Idea applications are well-suited for basic research/discovery science applications and have a lower threshold for the amount of preliminary data required compared to Development applications.

Development Award: US \$100,000 maximum Total Cost, 2-3 years in duration. Development applications have a higher threshold of preliminary data and are ideally suited for proposals with clear implications for therapeutic development.

For more info, visit barthsyndrome.org/research or email erik.lontok@barthsyndrome.org

Advocacy in Action

Barth Community Ambassadors Meet with Legislators

We at BSF express our heartfelt gratitude to Bryan D, Steven G and Walker B for recently meeting with legislators in their home States. All three volunteer ambassadors participated in a national campaign for better U.S. Food and Drug Administration (FDA) review processes for ultra-rare indications, like Barth syndrome.

Efforts by Bryan, Steve, and Walker were focused on greater transparency and consistency from the FDA, namely around the accelerated approval (AA) pathway, as it is crucial to Research and Development (R&D) efforts for Barth syndrome. This pathway allows the FDA to use a surrogate endpoint ("a marker, such as a laboratory measurement, radiographic image, physical sign or other measure that is thought to predict clinical benefit...") to evaluate the safety and efficacy of therapies for serious conditions with unmet needs. Use of this approach advances potential therapies much more quickly, though it often requires a follow-on study to confirm the expected benefit. It is tailor-made for diseases that are so rare, like Barth syndrome, that it is extremely difficult, if not impossible, to recruit an adequate number of patients to prove statistically that a potential drug is conclusively beneficial. (For additional information, visit EveryLife Foundation's website.)

Time is not a luxury for people with Barth syndrome, which makes the AA pathway a critical and ideal option for our community. Barth individuals continue to experience severely reduced quality of life and often death much too young and much too frequently. "I'm lucky to be here," said 35-year-old Steve G, "since so many people with this disease die very young.... If you are blessed enough to get to adulthood, you often require a heart



transplant or suffer from debilitating conditions [...] Taking two or three steps can cause shortness of breath, tiredness, and leg muscle pain."

New hope for a Barth-specific therapy emerged when Stealth BioTherapeutics (Stealth) conducted the first-ever clinical trial for Barth syndrome using elamipretide, a new drug to potentially treat the syndrome. Unfortunately, after several studies, the company received a refusal-to-file letter from the FDA in October 2021, meaning that their New Drug Application (NDA) had not been allowed to advance to the next step under the AA pathway or other regulatory approval mechanism. "It's incomprehensible that the drug has not been approved yet... I feel my words are falling on deaf ears with the FDA," said Walker B, a trial participant. "I've used terms like the "old Walker" vs the "new Walker" as I truly feel like a new person after being on an experimental therapy for more than 4 years [...] My energy, my

strength, my quality life, even just the way I look at life now has completely changed... I can't fathom life without this drug."

The inconsistent application of the AA pathway by regulators introduces unnecessary challenges and unpredictability in regulatory affairs for ultra-rare therapies, like elamipretide. It has also sparked the outrage of Barth constituents when the FDA defaulted to statistical requirements typical of larger indications for full regulatory approval. "We simply cannot comprehend why FDA holds ultra-rare disease populations to the same definitionally impossible standards as they do with diseases like cancer that affect tens and hundreds of thousands of people," said Bryan D, father of Abram who has Barth syndrome. "We need Accelerated Approval by the FDA to realize the first-ever life-enhancing therapy for our boys with Barth syndrome."

Much remains to be defined about the future of the AA pathway as well as the Barth

syndrome community's access to elamipretide. Just recently, Stealth announced that a new meeting had been granted by the FDA to discuss the potential therapy's future. We at BSF remain hopeful that the AA pathway will be actively considered as an option for elamipretide and all future therapies under development for ultra-rare diseases, and we will continue to work hard to make this a reality.

We again thank Bryan, Steve, and Walker and all those who are engaging on this vital issue. If you feel strongly that Barth syndrome deserves a chance at FDA, we encourage you to volunteer and become a State ambassador. Contact Shelley Bowen, BSF's Director of Family Services and Advocacy, if interested.

Alternatively, please reach out to your legislators through the TAKE ACTION links on the Barth Syndrome Foundation Legislative Advocacy webpage.

BSF Responds to FDA Granting Pre-NDA Meeting for Elamipretide to Stealth BioTherapeutics

In October 2021, Stealth BioTherapeutics (Stealth) received a refusal-to-file letter from the U.S. Food and Drug Administration (FDA) for the same proposed treatment in Barth syndrome. At present, there are no FDA-approved therapies for the treatment of Barth syndrome.

On June 14, 2022, Stealth announced that the FDA has granted the company a meeting to discuss a possible new drug application (NDA) for elamipretide as a potential treatment for Barth syndrome. The company intends to present new data collected during the Open Label Extension (OLE) period.

"With other potential treatments years away from the clinic, people in our community are in dire need of a safe, effective therapy that can potentially attenuate the devastating clinical outcomes and implications to quality of life for people living with this debilitating and life-threatening disease," said Emily Milligan, Executive Director of Barth Syndrome Foundation (BSF). "It is our hope that the FDA will review all available data this time that supports the approval of elamipretide as a potential therapy for Barth syndrome."

BSF at The Business of Rare Policy Summit

THE BUSINESS OF
RARE
POLICY SUMMIT
HOSTED BY KPM GROUP DC

INCENTIVES, INVESTMENTS & THE
WAY FORWARD FOR ULTRA RARE
DISEASE DRUG DEVELOPMENT

September 20, 2022
Hyatt Regency Capitol Hill
Washington, DC

SPEAKERS

Fireside Chat


Reenie McCarthy
President and CEO
Stealth BioTherapeutics




Emily Milligan
Executive Director
Barth Syndrome Foundation

New therapeutic opportunities are top-of-mind for all rare disease stakeholders, and very much so for the rare disease companies that are dedicated to responding to the urgent needs of rare disease patients.

But, it's not easy!

As part of BSF's ongoing advocacy efforts, Reenie McCarthy, president and CEO of Stealth BioTherapeutics, and Emily Milligan, executive director of BSF, discussed challenges and solutions for these issues at The Business of Rare Policy Summit on Tuesday, Sept 20th, in Washington DC. Both speakers cited experience with elamipretide in Barth syndrome and engaged regulators, industry, peer organizations, and legislators in discussion about private-public partnerships required to preserve and support the R&D landscape for rare diseases such as Barth syndrome.

Emily and Reenie shared the reality of ultra-rare drug development as a journey of discovery, where the lack of clinical development experience and regulatory precedent amplify the need for regulatory flexibility. "We want the FDA to think outside the box they are used to operating in," said Emily. The present challenges facing drug developers and advocacy organizations lie within the subjectivity of regulatory agencies. Guidance can be inconsistently applied and the statistical rigidity of the FDA in ultra-rare populations penalizes discovery in diseases where multiple trials may not be possible.

You can watch the recording of this talk at <https://youtu.be/Ky5AzwnlVuA>

FDA Regulatory Pathway Workshop

The Barth Syndrome Foundation (BSF), including BSF representatives as well as key clinical disease leaders, held an important workshop with Dr. Norman Stockbridge (Director of the Division of Cardiology and Nephrology in CDER at the FDA) and over 30 other representatives of different FDA centers, offices, and divisions on July 29, 2022. The stated purpose of this workshop was “to identify, through informed discussions, executable regulatory pathways for Barth syndrome therapy development and establish regulatory paths to approval.” It was a rare opportunity to further educate the FDA about disease-specific details of Barth syndrome and to initiate work that we hope ultimately will lead to consensus about possible paths forward for future approved treatments for our ultra-rare disease.

During the two-and-a-half-hour meeting, BSF leaders and several expert healthcare providers and researchers from around the world laid out details of the prevalence, diagnosis and clinical natural history of our disease. BSF also contextualized our discussion by highlighting advancements that our organization and affiliates have achieved in the last 22 years to become the single hub of information, as well as scientific and clinical activity, pertaining to Barth syndrome globally.

BSF and key opinion leaders provided important groundwork by recapping previously stated patient preferences along such dimensions as goals of treatment and tolerance of clinical benefit risk. To further set the framework, we also laid out aspects of our experiences with two drug trials that have been conducted in Barth syndrome so far. Finally, a brief synopsis of other ultra-rare disease regulatory history and

the implications of various FDA rules were presented by BSF’s regulatory consultant, James Valentine (who was also our expert moderator at BSF’s Patient Focused Drug Development [PFDD] meeting in 2018).

The workshop culminated in a lively and productive discussion about clinical endpoint selection, clinical trial design and possible regulatory pathways forward for future potential therapies in Barth syndrome. Many questions were raised by representatives from the FDA, and much fruitful and detailed brainstorming emerged.

Clearly, this was just the first incredibly important, but not sufficient, discussion among BSF patient advocates, Barth syndrome key opinion leaders, and FDA regulators that will be required to develop a consensus about these complicated, but absolutely critical, issues. BSF very much looks forward to continuing to work together through cross-sector collaborations to achieve our goal of defining viable and feasible paths towards regulatory approval of Barth syndrome therapies.

Neutropenia Educational Series

Neutropenia is a serious health risk because those who are neutropenic have an increased likelihood of developing life-threatening and potentially fatal sepsis. Chronic neutropenia is a life-long condition that one does not outgrow. Therefore, it is important to be aware of the risks of neutropenia while trying to maintain a balance in living a normal life. The key to this is to be educated about the risks and aware of treatment options for neutropenia. In so doing, the individual who has neutropenia as well as caregivers are equipped with the knowledge they need to make informed healthcare decisions.

The concerns associated with neutropenia can change over time. The primary concerns a parent would have for an infant child with neutropenia shift as the child grows older and begins to engage differently with the world. Eventually the child needs to become an advocate for their own health. Therefore, it is important to pave the way through this transition process so that the young adult is prepared to make informed healthcare decisions about their own health.

The National Neutropenia Network and the Barth Syndrome Foundation have been hosting a neutropenia educational series that will continue through November 2022. We invite you to join us as we learn about neutropenia from experts who will focus on the specific concerns patients and parents have expressed about living with or raising a child who suffers with this lifelong condition. Recordings of all sessions will be available on BSF’s website.

Tweens and Teens with Neutropenia (10 to 18 years)

Thursday, Aug. 25th, 2022, 12:00 PM ET Recording Available [HERE](https://qrco.de/recordings) <https://qrco.de/recordings>
Thomas Michniacki, MD, Clinical Assistant Professor, Pediatric Hematology and Oncology, C.S. Mott Children’s Hospital, Ann Arbor, MI
Liam Lakhia, Neutropenia Patient and Patient Advocate, Cincinnati, OH

School Age Children with Neutropenia (4 to 10 years)

Friday, Sep. 23rd, 2022, 12:00 PM ET Recording Available [HERE](https://qrco.de/recordings) <https://qrco.de/recordings>
James A. Connelly, MD, Pediatric Hematology and Oncology, Vanderbilt University Medical Center, Nashville, TN
Tammy Loader, Parent and Patient Advocate, Cambridge, OH

Newborns Infants Toddlers and Preschoolers with Neutropenia (0 to 4 years)

Thursday, Oct. 27th, 2022, 12:00 PM ET Registration Link [HERE](https://qrco.de/neut0-4reg) <https://qrco.de/neut0-4reg>
Jolan Walter, MD, PhD, FAACAP, Robert A. Good Endowed Chair, Pediatric Allergy and Immunology, University of South Florida, Tampa, FL
Kelly Jo Walkovich, MD, Clinical Associate Professor, Pediatric Hematology and Oncology, C.S. Mott Children’s Hospital, Ann Arbor, MI

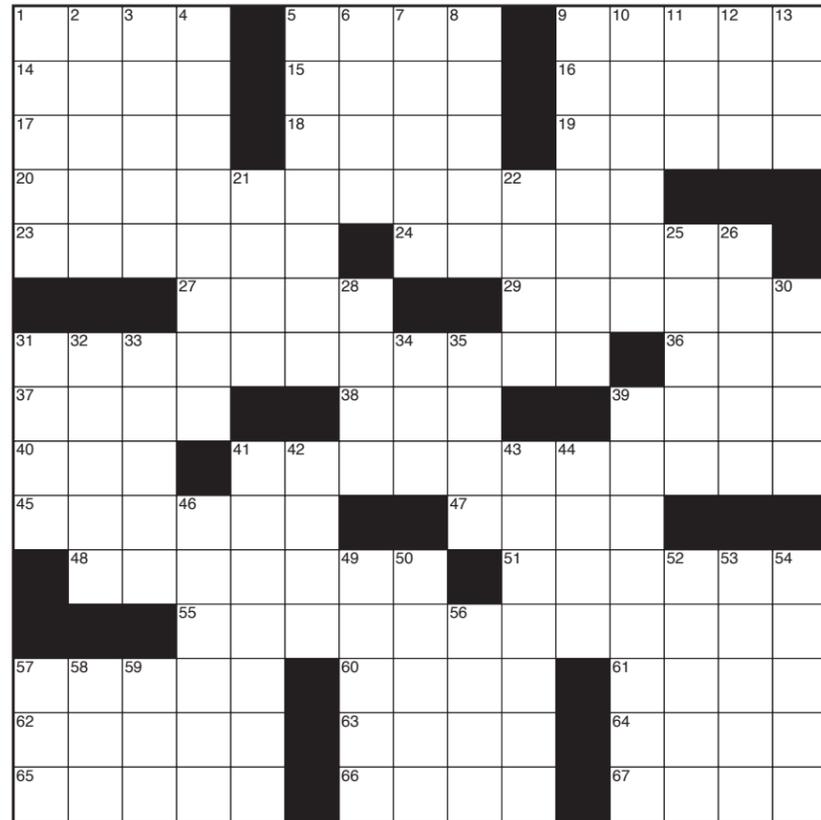
Adults with Neutropenia (18 + years)

Friday, Nov. 18th, 2022, 12:00 PM ET Registration Link [HERE](https://qrco.de/neutadultreg) <https://qrco.de/neutadultreg>
Eric Scott, PhD, Clinical Associate Professor, Pediatric Psychology, C.S. Mott Children’s Hospital, Ann Arbor, MI
Heidie Rothschild, DHSc, MHA, BS FACCP, Neutropenia Patient and Patient Advocate, Baltimore, MD

Community Crossword



2005 Palmer Avenue #1033
Larchmont, New York 10538



ACROSS

- 1 Where Barth Italia families might ski
- 5 Bar found in the tub
- 9 Dr. Anthony who knows a lot about COVID-19
- 14 Move, in Realtor lingo
- 15 Blue Jay or Oriole, but not a Cardinal
- 16 Prefix for -sphere
- 17 Shape of many pills
- 18 Furry biped in the Himalayas
- 19 Michael Keaton played this stay-at-home dad in 1983
- 20 Organelle affected in Barth syndrome
- 23 St. Francis of ____
- 24 Related to the Greek god of wind
- 27 Exams taken by HS juniors and seniors in the US
- 29 Slight tints
- 31 Low white blood cell count in Barth syndrome

- 36 Gun an engine
- 37 Olive and her family
- 38 Doce meses
- 39 Broad
- 40 Title of one who's done with the USMC?
- 41 Phospholipid affected in Barth syndrome
- 45 Bit of food
- 47 Winnebago enthusiast
- 48 Symptom often felt by patients with Barth syndrome
- 51 Like paradise
- 55 Drug said to improve symptoms in Barth syndrome, aka SS-31

- 57 It's also known as a zebra giraffe
- 60 Our Barth UK patients might like these "mushy"
- 61 Figure skating jump New car that's gone sour?
- 63 Ireland: Var.
- 64 Bell sound
- 65 Watching warily
- 66 What grandparents often do with grandchildren
- 67 Snake's sounds

DOWN

- 1 What might waft from a patisserie
- 2 Brand of jeans
- 3 Braids
- 4 Singers of arias, usually
- 5 Greet your friend
- 6 Margarine
- 7 Health insurance giant
- 8 Lions' group
- 9 Padres y ninos
- 10 Duke Ellington would like you to take this!
- 11 Expression of hesitancy
- 12 Sound of love or dove
- 13 Doctrine
- 21 Old Russian ruler: Var.
- 22 Indian flatbread
- 25 "Get ____!"
- 26 "____ remind you..."
- 28 Shadow box
- 30 "The Governor" in the movie Cars
- 31 Usual, standard
- 32 "____ the Tiger" (theme to Rocky III)
- 33 ____ sound: The basis for an echocardiogram
- 34 Finish
- 35 When children in France usually sleep
- 39 Secretive listening-in ons
- 41 Floor to ____
- 42 That green scum you find in ponds
- 43 Supervise
- 44 First bit of a breaking news story
- 46 "____ it!" (Move!)
- 49 Called strikes and balls
- 50 What Old McDonald yelled?
- 52 Says no to
- 53 Outputs from brains
- 54 Basic units of life
- 56 Split hairs?
- 57 Cry heard at the World Cup
- 58 ____ Largo
- 59 Friend in L'association Syndrome de Barth



Thank you to Dr. Colin Phoon for creating this crossword puzzle for our community! You can find the answer key to the puzzle by visiting <https://bit.ly/barthpuzzle>