Barth Syndrome Foundation®

2005 Palmer Ave., #1033
Larchmont, New York 10538
Phone: 914-303-6323

www.barthsyndrome.org

What is **Barth syndrome**?

Ultra-rare, life-threatening, genetic mitochondrial disorder, affecting ~150 individuals across the U.S.

- Barth syndrome is caused by pathological changes in the TAFAZZIN gene.
- Similar to Duchenne Muscular Dystrophy, Barth syndrome affects mostly males as TAFAZZIN is on the X chromosome.
- There are **no FDA-approved treatments** for Barth syndrome.

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

Last Updated: June 16, 2025

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Regulatory Delays Cost Time, Money, & ***Lives***

Our Journey:

- **>10 year journey** to get 1st drug, **elamipretide**, for Barth syndrome reviewed. 4 listening sessions with FDA were held.

Continued Challenges:

- Despite priority review designation, assigned a standard review timeline *adding a 6+ month delay*
- PDUFA date then further **delayed by additional 3 months**
- A 6-month priority review took **>15 months**
- **~200** information requests for a 12-person trial *since* Oct. 2024
- **~80** additional analyses requested in Feb. 2025
- Despite a favorable Advisory Committee ruling, FDA issued a CRL in May 2025; FDA suggested resubmission via accelerated approval adding time, cost, uncertainty and the **exclusion of infants**

The Costs:

- 10% of the Barth syndrome community has died
- 18% have required heart transplants
- Exorbitant costs to drug Sponsor and Barth Syndrome Foundation
- Reduced Biopharma interest in rare disease

Our Ask:

Please write to FDA and ask for no further delays.

Our community has already waited too long.

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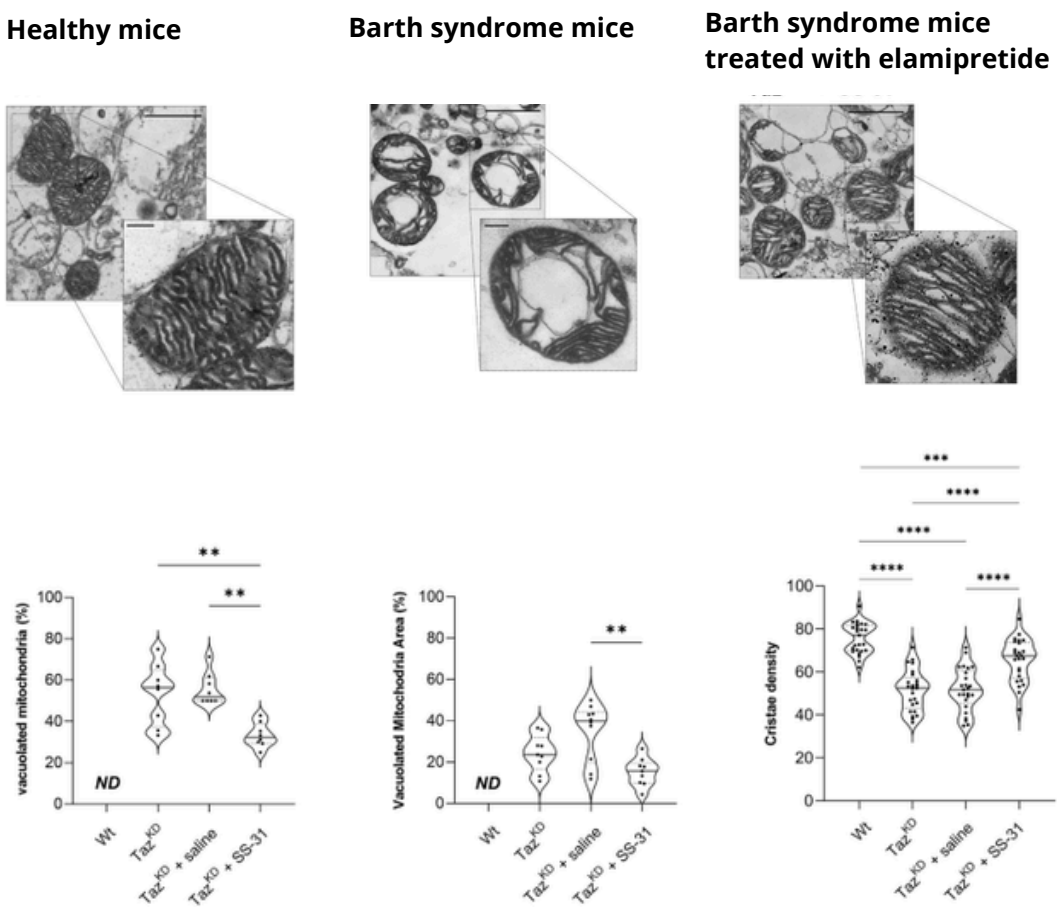
What is **elamipretide?**

Elamipretide

- First-in-class, mitochondrial targeted peptide
- In development for diseases of mitochondrial dysfunction including Barth syndrome & dry age-related macular degeneration (dry AMD)

Impact on Mitochondria

- Mitochondria provide cells with energy
- Defective mitochondria make less energy for cells and exhibit other cellular defects that impact tissues like the heart and skeletal muscle that contain large numbers of mitochondria
- In Barth syndrome, where TAFAZZIN is mutated, mitochondria are dysfunctional, misshaped and cannot provide enough energy
- Elamipretide restores mitochondrial shape and improves function



Russo, De Rasmo, Rossi, Signorile, & Lobasso Sci Rep (2024)

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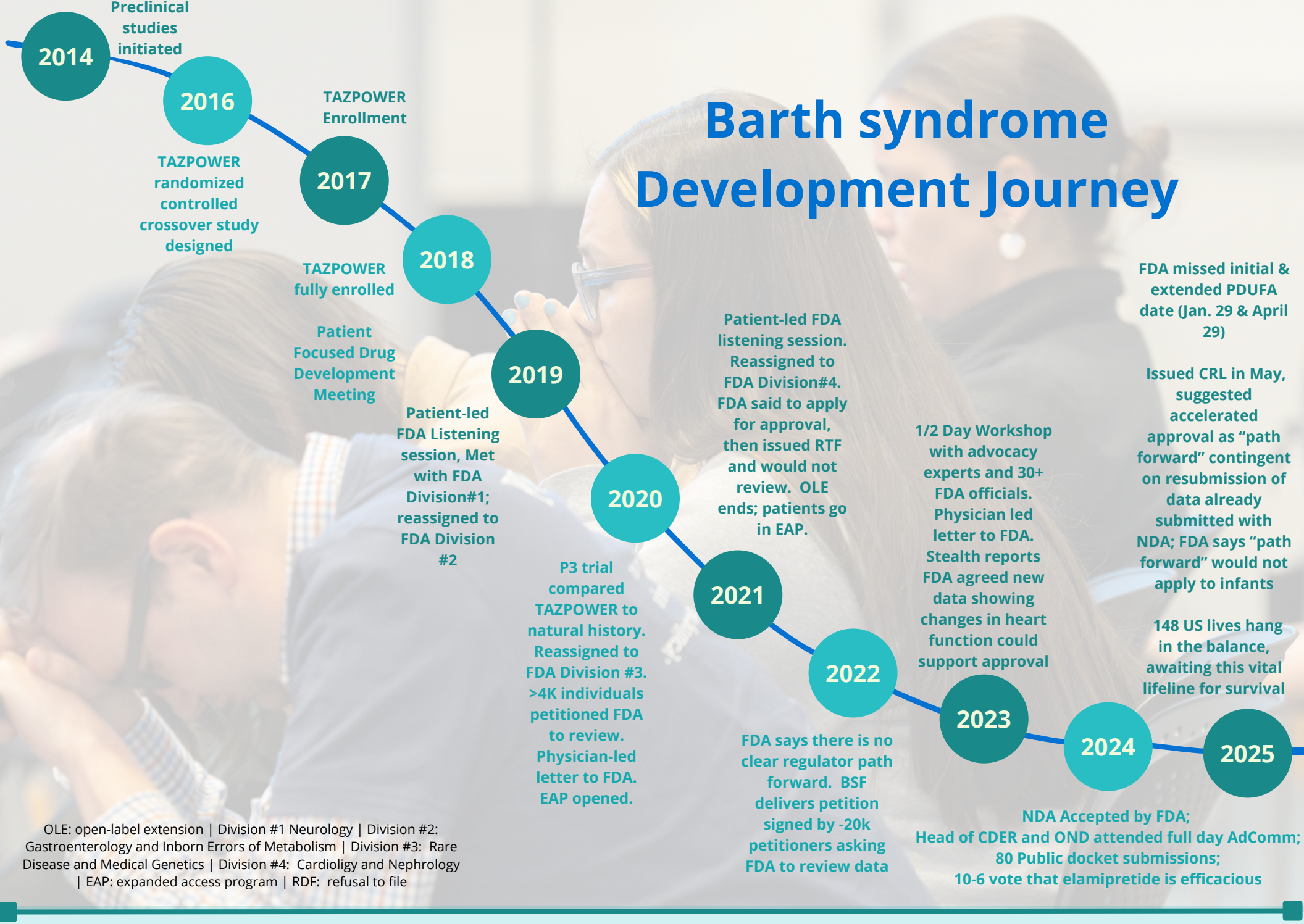
Barth syndrome Development Journey



2014 — Preclinical studies initiated

2016 — TAZPOWER randomized controlled crossover study designed

2017 — TAZPOWER Enrollment

2018 — TAZPOWER fully enrolled

Patient Focused Drug Development Meeting

2019 — Patient-led FDA Listening session, Met with FDA Division#1; reassigned to FDA Division #2

2020 — P3 trial compared TAZPOWER to natural history. Reassigned to FDA Division #3. >4K individuals petitioned FDA to review. Physician-led letter to FDA. EAP opened.

2021 — Patient-led FDA listening session. Reassigned to FDA Division#4. FDA said to apply for approval, then issued RTF and would not review. OLE ends; patients go in EAP.

2022 — FDA says there is no clear regulator path forward. BSF delivers petition signed by -20k petitioners asking FDA to review data

2023 — 1/2 Day Workshop with advocacy experts and 30+ FDA officials. Physician led letter to FDA. Stealth reports FDA agreed new data showing changes in heart function could support approval

2024 — FDA missed initial & extended PDUFA date (Jan. 29 & April 29)

Issued CRL in May, suggested accelerated approval as "path forward" contingent on resubmission of data already submitted with NDA; FDA says "path forward" would not apply to infants

148 US lives hang in the balance, awaiting this vital lifeline for survival

2025 — NDA Accepted by FDA;
Head of CDER and OND attended full day AdComm;
80 Public docket submissions;
10-6 vote that elamipretide is efficacious

OLE: open-label extension | Division #1 Neurology | Division #2: Gastroenterology and Inborn Errors of Metabolism | Division #3: Rare Disease and Medical Genetics | Division #4: Cardiology and Nephrology | EAP: expanded access program | RDF: refusal to file

Patients understand their critical role and have clearly stated that they want a chance to try a safe therapy.

~ Kate McCurdy, BSF Board Chair

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