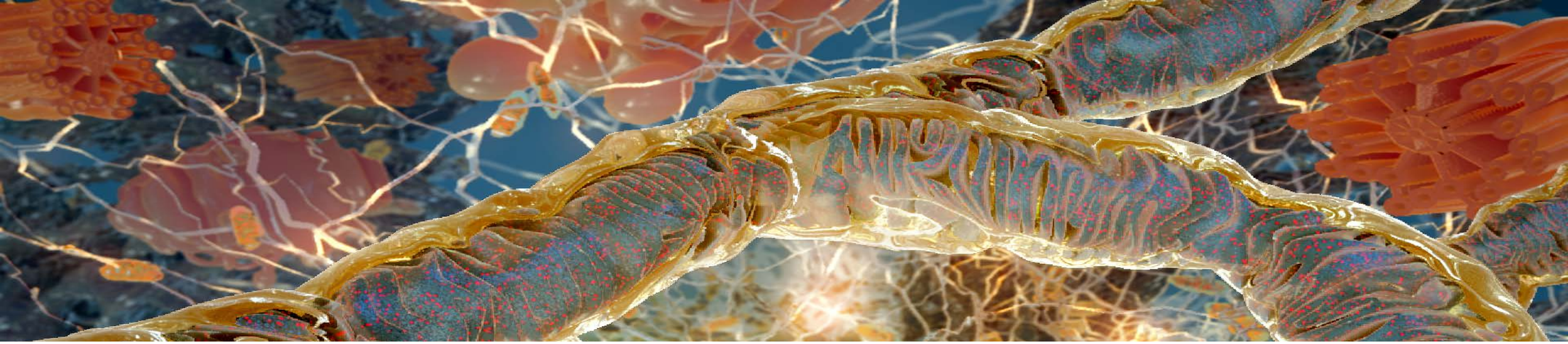

Targeting bioenergetic dysfunction across human disease

Stealth BIOTHERAPEUTICS

Leading Mitochondrial Medicine

February 2022

Our forward-looking statements and disclaimers

This presentation and various remarks we make during this presentation contain forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995. Such forward-looking statements include those regarding Stealth BioTherapeutics' plans, strategies and expectations for its preclinical and clinical advancement of its drug development programs, including its ongoing clinical trials of elamipretide and planned clinical trial of SBT-272; its expectations regarding regulatory interactions,; the potential benefits of Stealth BioTherapeutics' product candidates; its key milestones for 2022; and its plans regarding future data presentations. Statements that are not historical facts, including statements about Stealth BioTherapeutics' beliefs, plans and expectations, are forward-looking statements. The words "anticipate," "expect," "hope," "plan," "potential," "possible," "will," "believe," "estimate," "intend," "may," "predict," "project," "would" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Stealth BioTherapeutics may not actually achieve the plans, intentions or expectations disclosed in these forward-looking statements, and you should not place undue reliance on these forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements as a result of known and unknown risks, uncertainties and other important factors, including: Stealth BioTherapeutics' ability to obtain additional funding and to continue as a going concern; the impact of the COVID-19 pandemic; the ability to successfully demonstrate the efficacy and safety of Stealth BioTherapeutics' product candidates and future product candidates; the preclinical and clinical results for Stealth BioTherapeutics' product candidates, which may not support further development and marketing approval; the potential advantages of Stealth BioTherapeutics' product candidates; the content and timing of decisions made by the FDA, the EMA or other regulatory authorities, investigational review boards at clinical trial sites and publication review bodies, which may affect the initiation, timing and progress of preclinical studies and clinical trials of Stealth BioTherapeutics product candidates; the possibility that the FDA will not file the Barth NDA; Stealth BioTherapeutics' ability to obtain and maintain requisite regulatory approvals and to enroll patients in its planned clinical trials; unplanned cash requirements and expenditures; competitive factors; Stealth BioTherapeutics' ability to obtain, maintain and enforce patent and other intellectual property protection for any product candidates it is developing; and general economic and market conditions. These and other risks are described in greater detail under the caption "Risk Factors" included in the Stealth BioTherapeutics' most recent Annual Report on Form 20-F filed with the Securities and Exchange Commission ("SEC"), as well as in any future filings with the SEC. Forward-looking statements represent management's current expectations and are inherently uncertain. Except as required by law, Stealth BioTherapeutics does not undertake any obligation to update forward-looking statements made by us to reflect subsequent events or circumstances.

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Pioneering mitochondrial medicine

Ophthalmology

- **Dry age-related macular degeneration** (dry AMD) P2b data Q2 2022; intravitreal formulation development ongoing

Neuromuscular/Neurology

- **nDNA-related primary mitochondrial myopathy** (nPMM) P3 clinical trial recruiting
- **Duchenne muscular dystrophy** IND submission planned
- **SBT-272** preclinical evidence of improved survival and neuronal health in **amyotrophic lateral sclerosis (ALS)** models; P1 trial initiation planned H1 2022
- **SBT-550** series improved cell-survival in **Friedreich's ataxia** patient-derived fibroblasts

Cardiology

- **Barth syndrome** FDA feedback on proposed new trial or animal studies expected Q1 2022

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Our pipeline

Indication	Drug	Discovery	Preclinical	Phase 1	Phase 2	Phase 3
Geographic atrophy (GA) in dry age-related macular degeneration (AMD)	Elam	→	→	→	→	*Data expected Q2 2022*
Primary mitochondrial myopathy due to nDNA mutations (nPMM)	Elam	→	→	→	→	*P3 study recruiting*
Duchenne muscular dystrophy (DMD)	Elam	→	→	→	*IND submission planned*	
Barth Syndrome	Elam	→	→	→	→	→
Neurology pipeline	SBT-272	→	→	*Toxicology studies ongoing; P1 initiation H1 2022; evaluating for amyotrophic lateral sclerosis (ALS) and frontotemporal dementia (FTD)*		
Neurology pipeline	SBT-550 series	→	*Evaluating for Friedreich's ataxia, Leigh's syndrome*			

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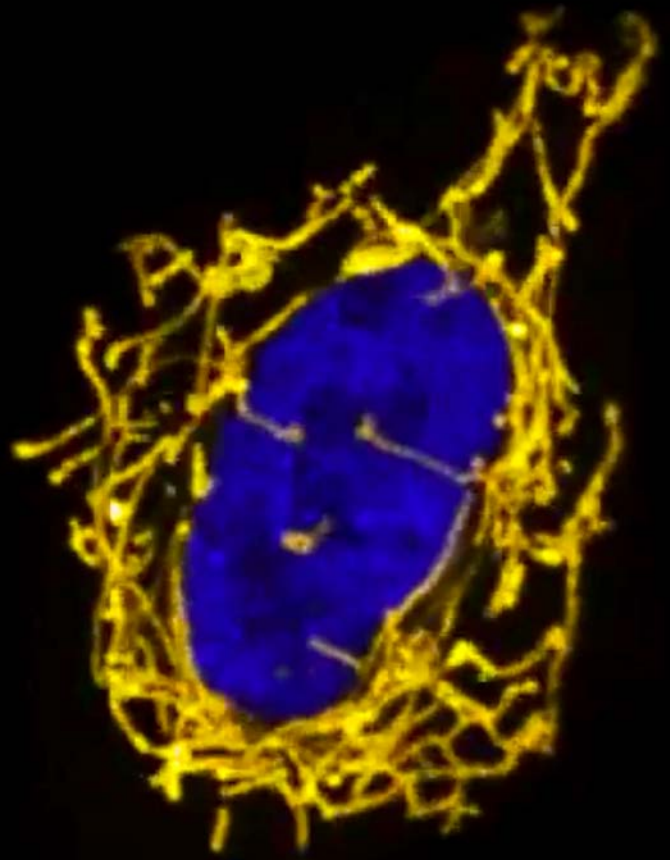
Mitochondrial dysfunction and human disease



Dr. Dylan Burnette (@mag2art), Vanderbilt Univ

- Mitochondria produce ~90% of the energy utilized by mammalian cells through a highly dynamic mitochondrial network
- Mitochondrial oxidative stress is implicated across many rare and common diseases, typically involving organ systems with high energy demands (eye, skeletal muscle, heart, brain)
- First-in-class lead compound, elamipretide, has shown clinical benefit in ophthalmic, skeletal muscle and cardiac diseases. SBT-272 (clinical stage) and first-in-class SBT-550 series (preclinical) are in development for neurological diseases.

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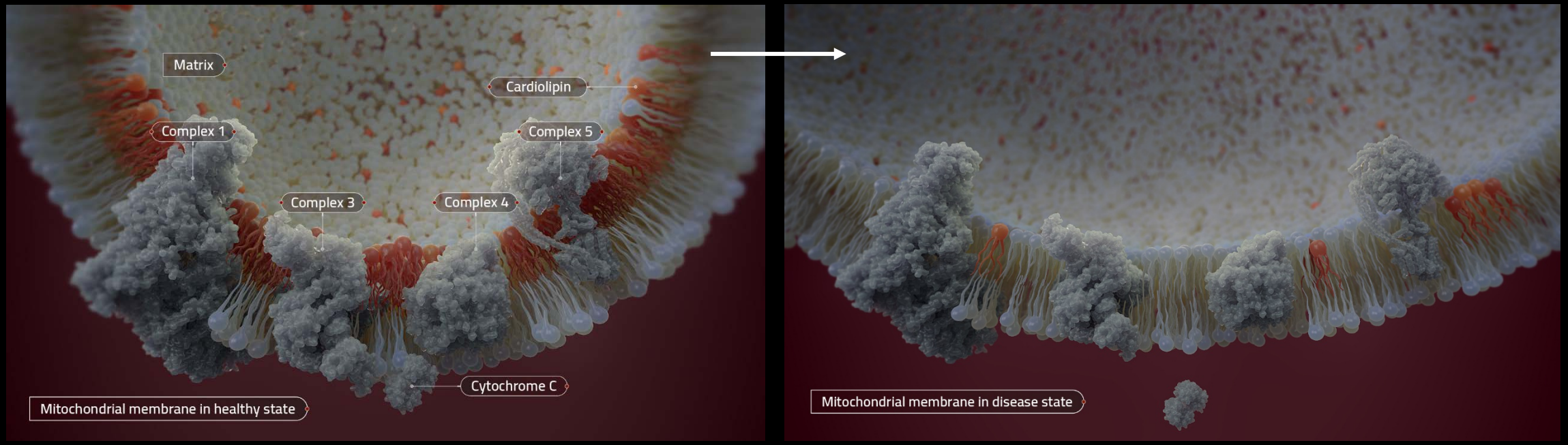
Mitochondrial inner membrane is disrupted in disease

In healthy states, cardiolipin promotes inner mitochondrial membrane curvature to organize respiratory complexes

ROS-mediated damage of cardiolipin disrupts cristae curvature and organization of respiratory complexes



Wang et al., PNAS 2019

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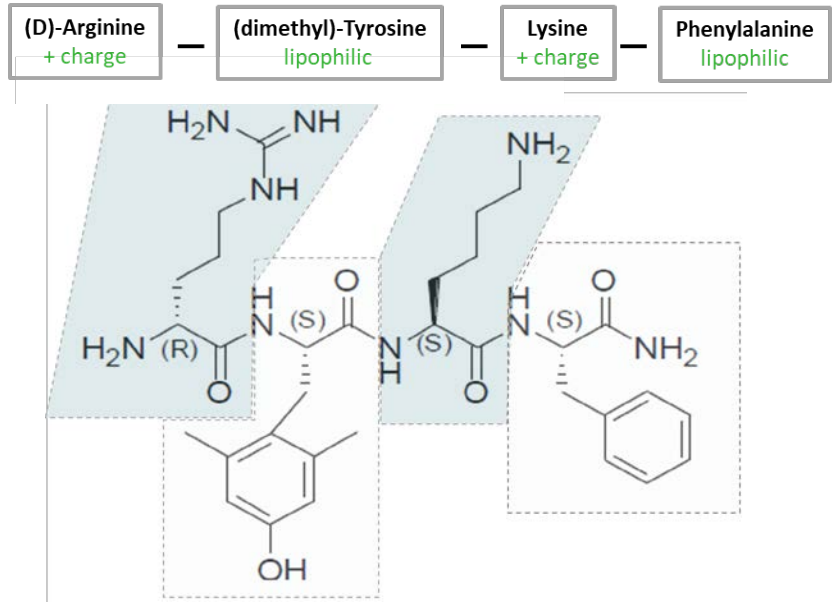
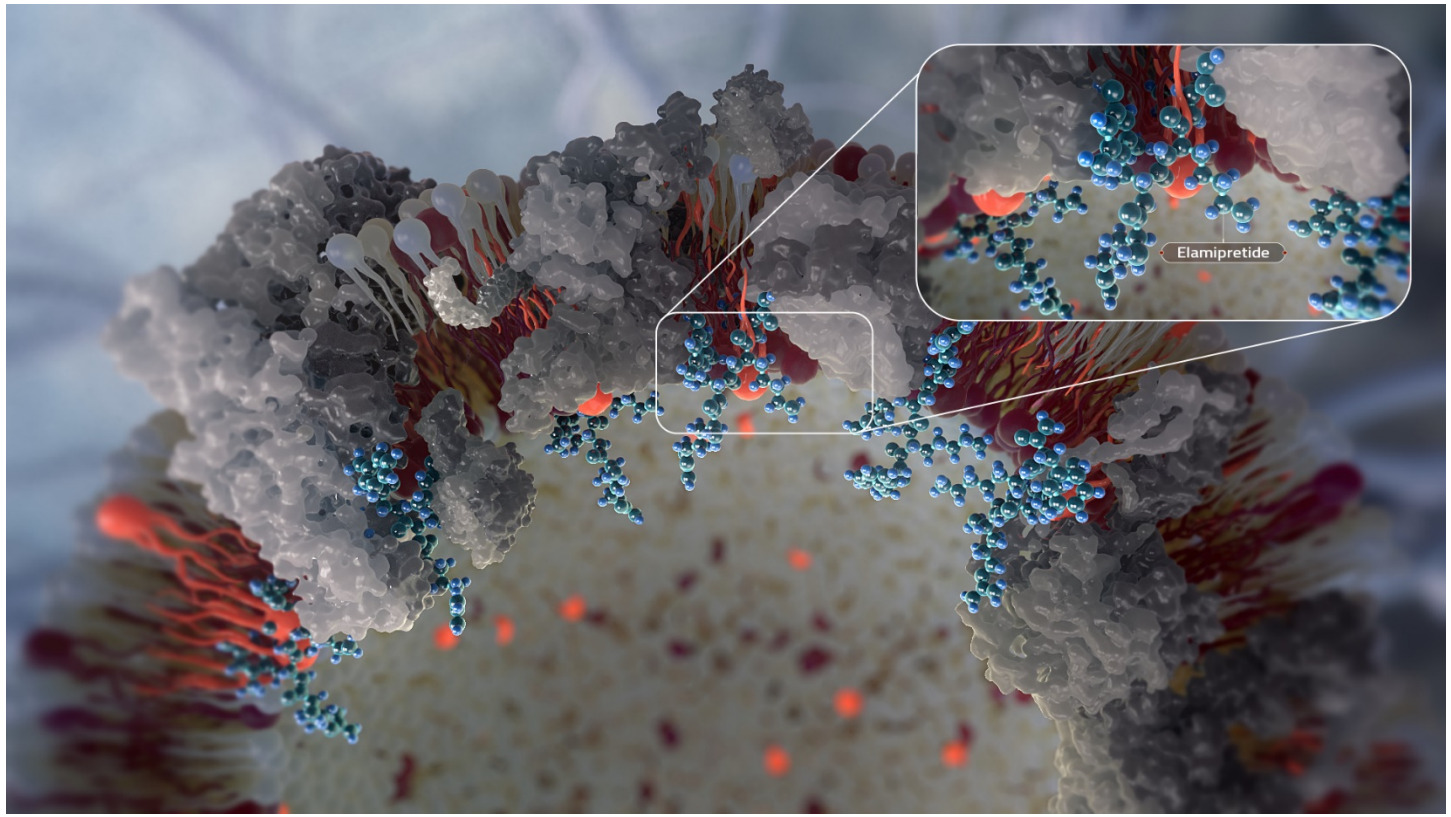
Elamipretide targets cardiolipin; improves IMM structure

Elamipretide modulates IMM dynamics which are disrupted in diseases entailing mitochondrial dysfunction



Charge motif optimizes mitochondrial targeting



Positively charged residues interact electrostatically with CL anionic headgroups, nonpolar side chains penetrate IMM gaps to interact hydrophobically with CL acyl chains, improving lipid packing, cristae morphology and IMM surface area[1]

IMM = inner mitochondrial membrane; CL = cardiolipin

[1] Mitchell, Wayne et al. "The mitochondria-targeted peptide SS-31 binds lipid bilayers and modulates surface electrostatics as a key component of its mechanism of action." The Journal of biological chemistry vol. 295,21 (2020): 7452-7469. doi:10.1074/jbc.RA119.012094

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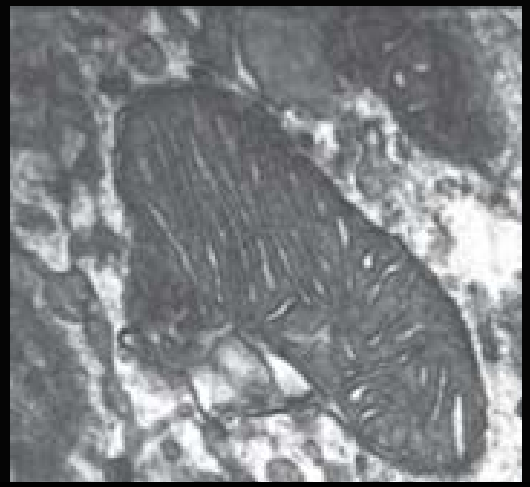
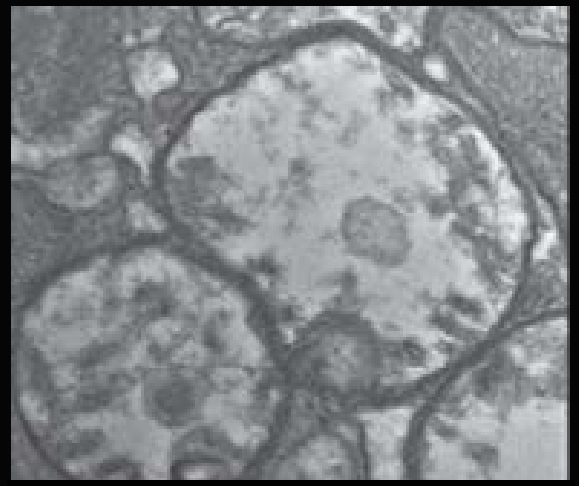
Elamipretide normalizes morphology, networking

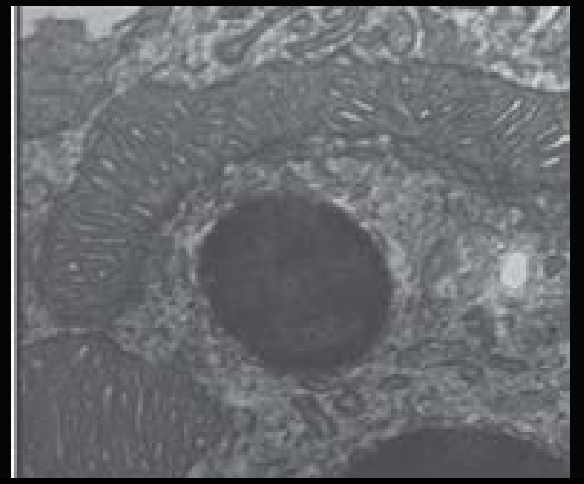
Improved morphology in mouse model of diabetic retinopathy



Normal mouse

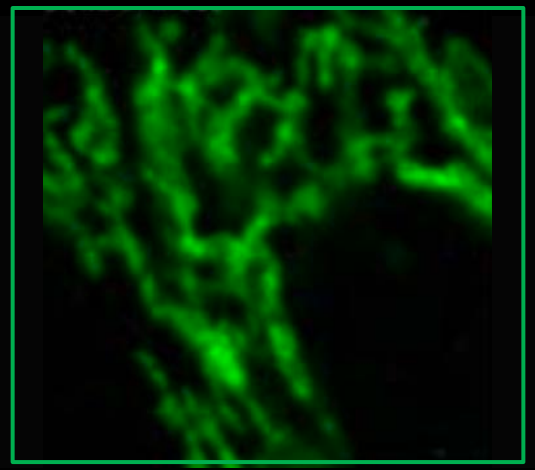


Placebo-treated diabetic mouse

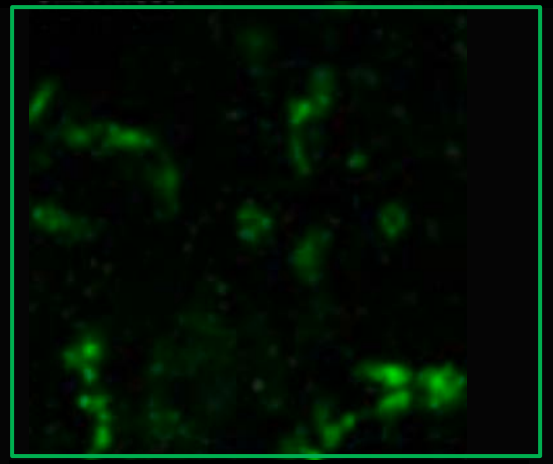


Elamipretide-treated diabetic mouse

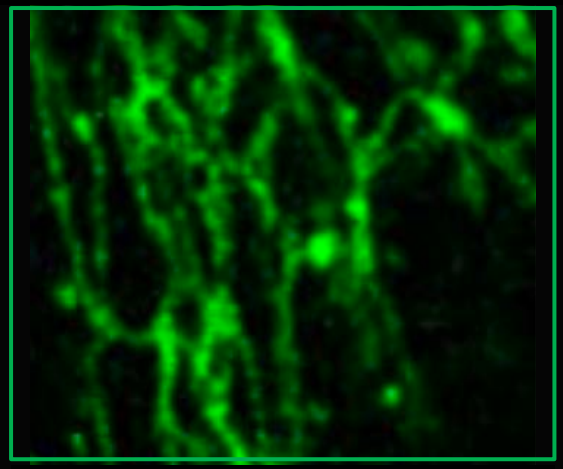
Improved networking in DCMA patient derived cells



Normal



Cardiomyopathy



Cardiomyopathy + elamipretide

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Szeto, Birk, Am J Physiol 2014 Szeto HH, Birk AV. Clin Pharmacol Ther. 2014

Wang et al., PNAS 2019

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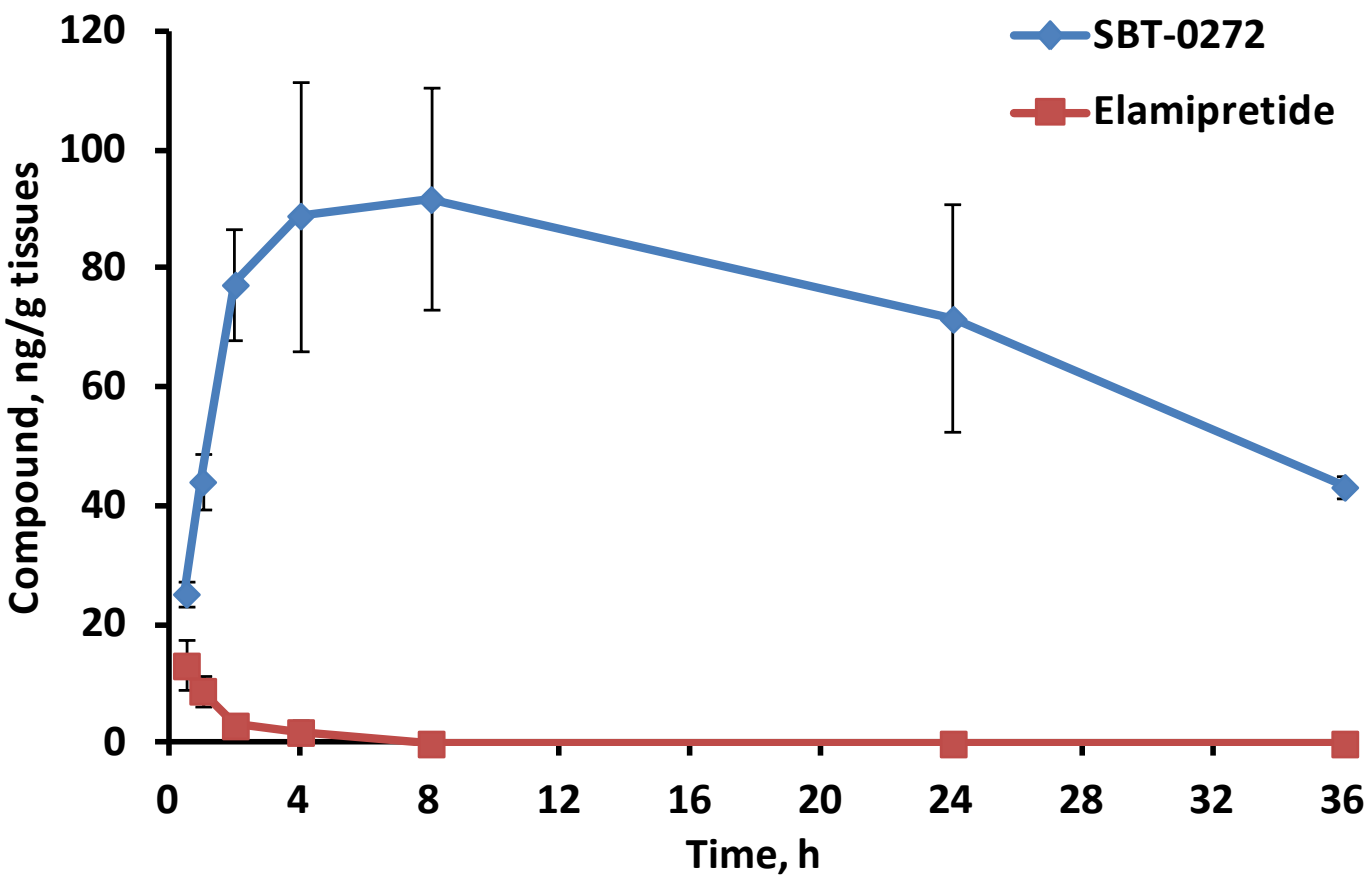
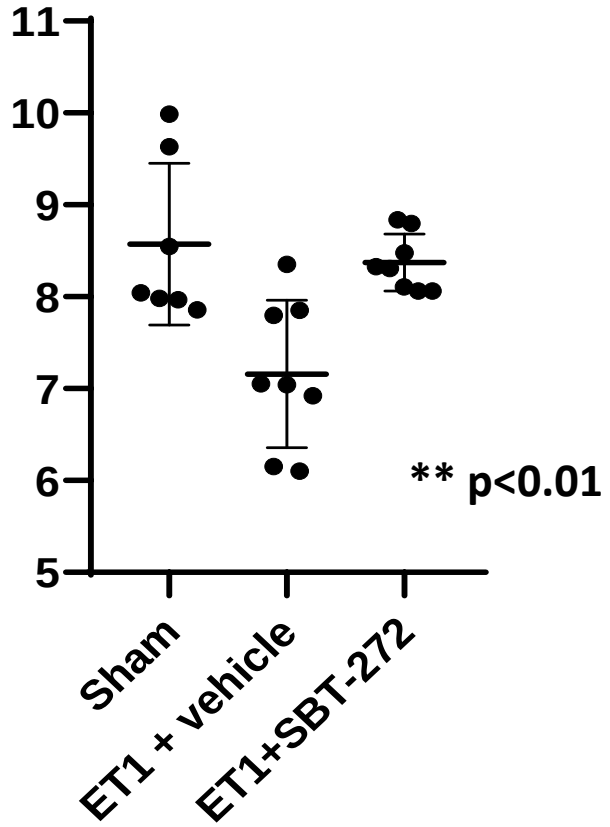
SBT-272 optimized for neurological diseases

Brain exposure: SBT-272 vs. Elamipretide



Improved Respiratory Control Ratio after Cerebral Ischemia/Reperfusion



Stealth BT data on file; showing brain accumulation in Sprague Dawley after 5mg/kg SBT-272 or elamipretide (n=4 per time-point).

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Ophthalmology

*Dry AMD ~2 million**

- *Fast track designation*

Preclinical efforts in glaucoma underway

The visual system is one of the most energy-demanding systems in the brain.

The visual system is particularly vulnerable to functional deficits induced by deficiencies in energy metabolism.

Defects in energy metabolism often lead to visual deficits and even blindness in diseases such as age-related macular degeneration (AMD), glaucoma and diabetic retinopathy, as well as genetic diseases such as LHON and FRDA.

Ophthalmology Scientific Advisory Board: Jeffrey Heier, MD, Chair; David Boyer, MD; David Brown, MD; Peter Kaiser, MD; Phil Rosenfeld, MD

* All estimates are of US patients affected

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Dry age-related macular degeneration

'You feel very insecure out of doors. You can't see the edges of pavements. People whizzing past you on bicycles on the pavement are a nightmare… You have this tendency not to panic but to get into a sort of mini panic situation especially when you don't know where you are… Also crossing a road, no matter how used you are, when you get to the other side your heart is racing which is, you know, odd. You can't help tensing up. You feel very vulnerable.'

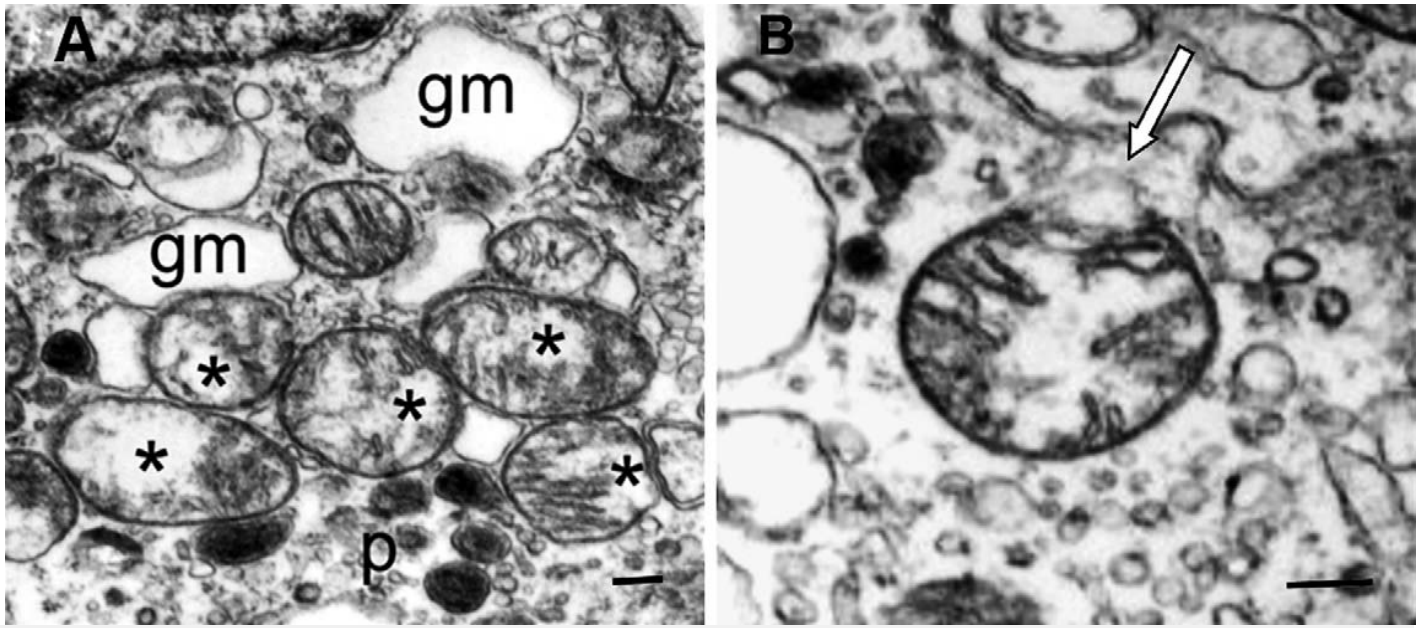
leading cause of blindness
in older adults

major contributor to
loss of independence

no approved therapies

Taylor, et al., Eye, 2019; Casten et a.., Psych. Times, 2006; Brightfocus.org; Lancet

Characterized by marked mitochondrial defects



Electron microscopy of mitochondrial abnormalities in AMD (84-year-old female)

- Extensive loss of cristae and matrix density (*)
- "Ghost" mitochondria (gm)
- Mitochondrial dissolution with bleb formation (arrow) on the internal and external membranes

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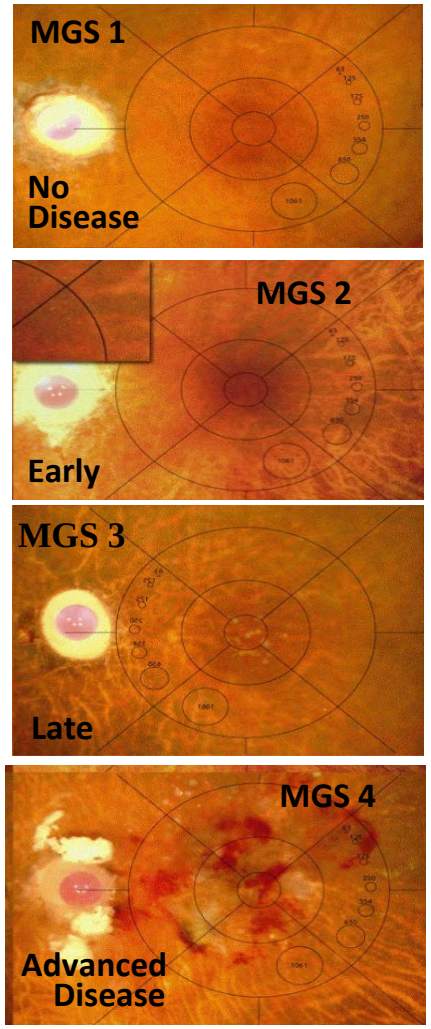
RPE mtDNA Damage Increases with AMD Progression

Minnesota Grading System

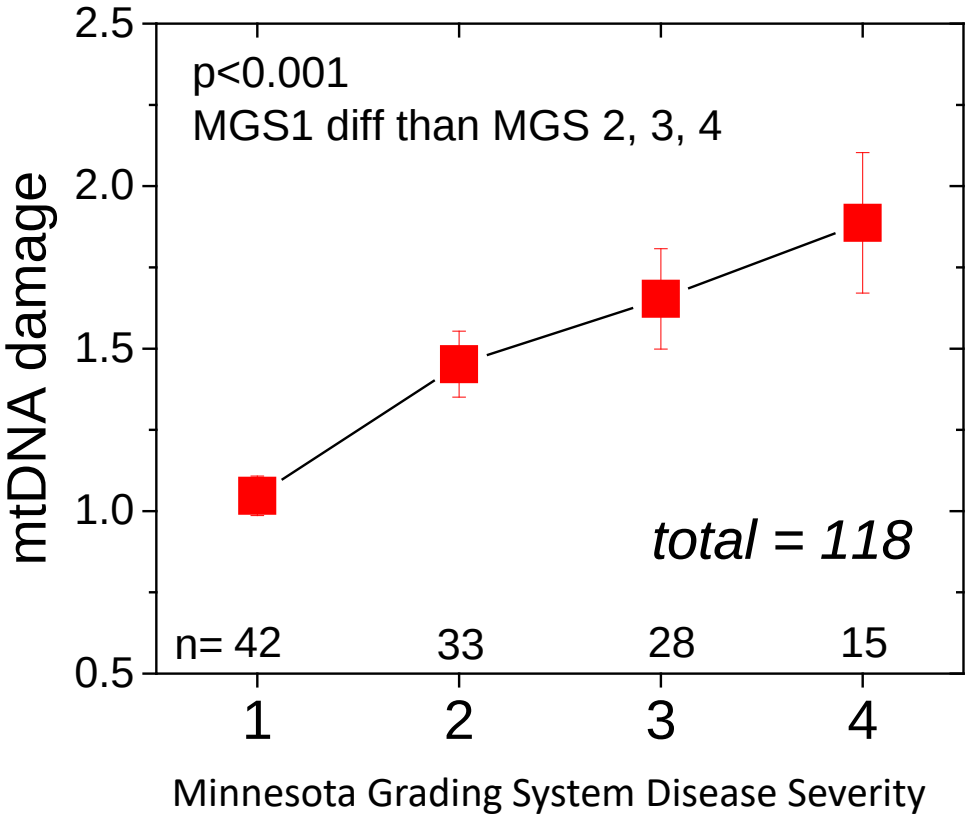


Control

Drusen/ RPE Pigment Changes

CNV/GA Vision Loss

Frequency of mitochondrial DNA lesions as a function of AMD disease severity



Mitochondrial DNA damage is significantly increased in the RPE of patients with AMD

Minnesota Grading System (MGS), Olsen and Feng, IOVS, 2004; Decanini et al., Am J Ophthalmol 2007
Combined data from Karunadharma, et al., IOVS, 2010; Terluk et al., J Neuroscience, 2015

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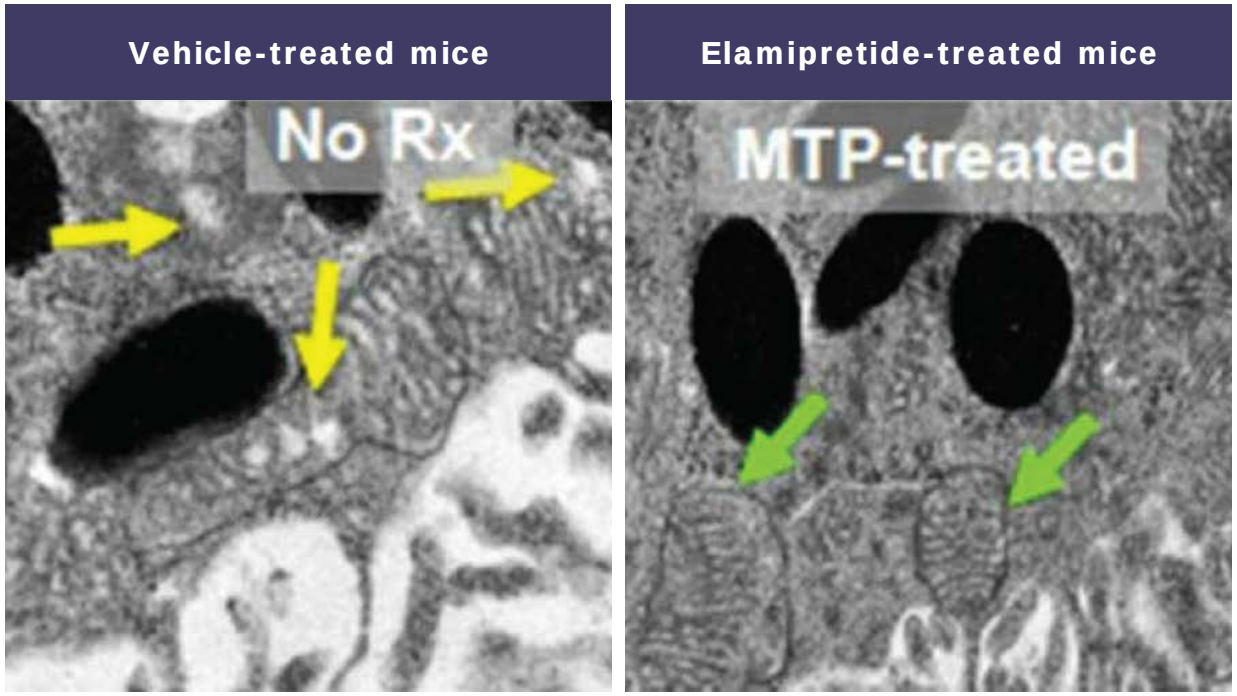
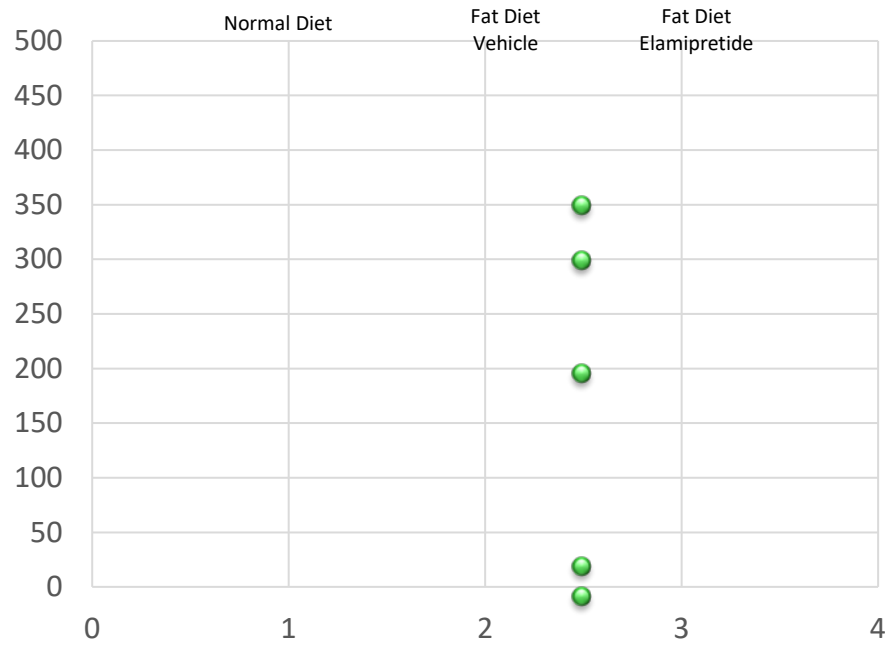
Mitochondrial ultrastructure protection in dAMD models

Electron microscopy of retinal tissue from mice receiving subconjunctival hydroquinone (HQ) injection



Comparison of B-wave amplitudes in APOE4 mice



Elamipretide prevents HQ-induced mitochondrial vacuolization

Elamipretide also improved vision in this model

Cousins SW. Role of mitochondrial dysfunction in dry age-related macular degeneration. *Retina Today*. May/June 2015.

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ReCLAIM Phase 1 trial in dAMD

- Low light or nighttime visual dysfunction is an early sign of dry AMD and a primary endpoint for ReCLAIM-2, our Phase 2 trial
- Patients were screened for a ≥5-letter low-light deficit
- Trial enrolled 40 patients with extra-foveal geographic atrophy (GA) (n=19) and high risk drusen (n=21)
- After 6 mos. of once daily 40 mg SC elamipretide therapy, change was assessed from baseline (BL) in all subjects who completed (n=15 GA; n=19 drusen)

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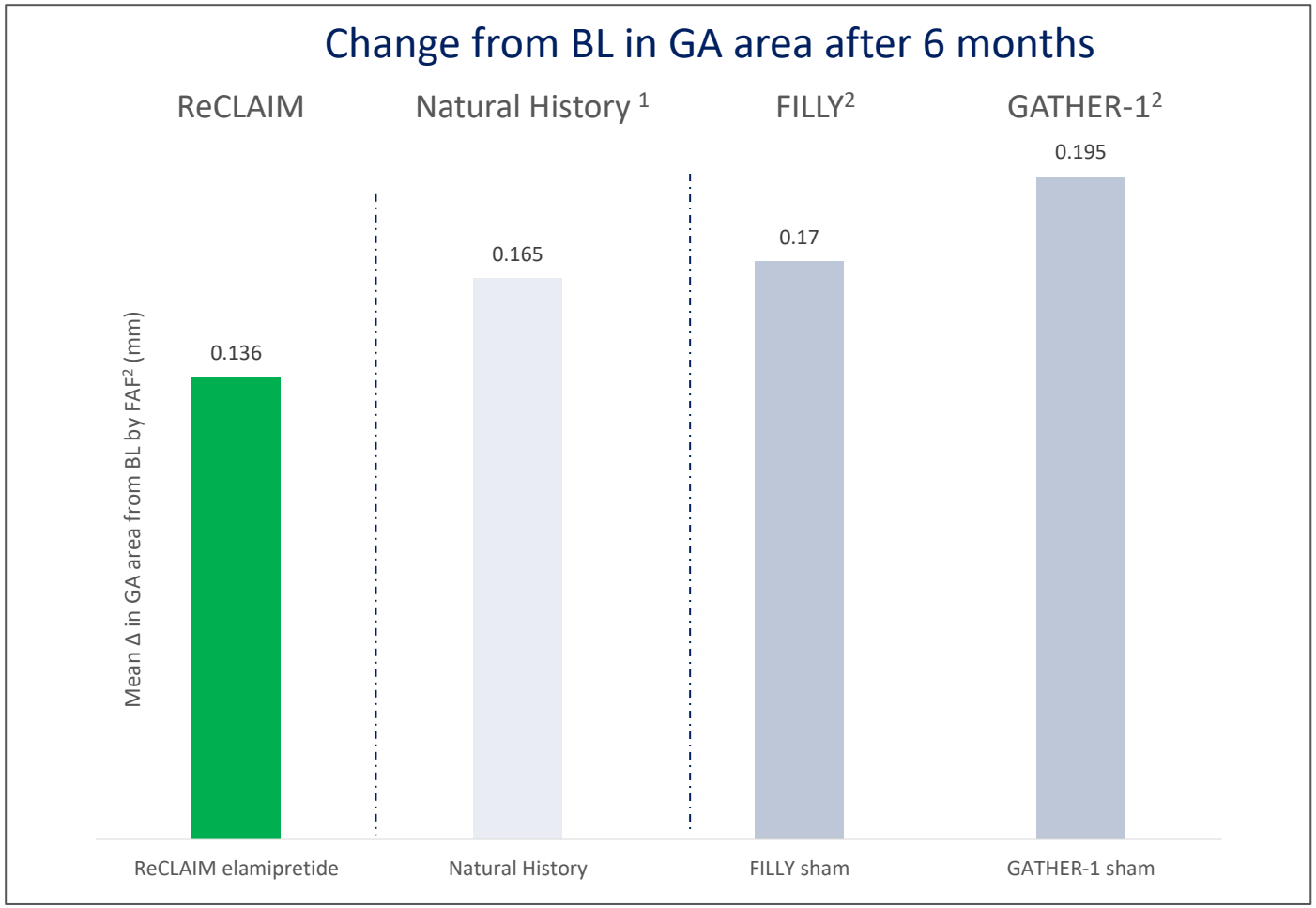
Slowed GA growth relative to natural history



1 Wang J, 2020. Ophthalmic Res.

2 Liao et al., Ophthalmology 2020; Jaffe et al., Ophthalmology 2020

FILLY and Gather-1 patient populations differ from ReCLAIM. FAF^2=fundus autofluorescence, square root; LLVA=low light visual acuity; Δ=change; BL= baseline

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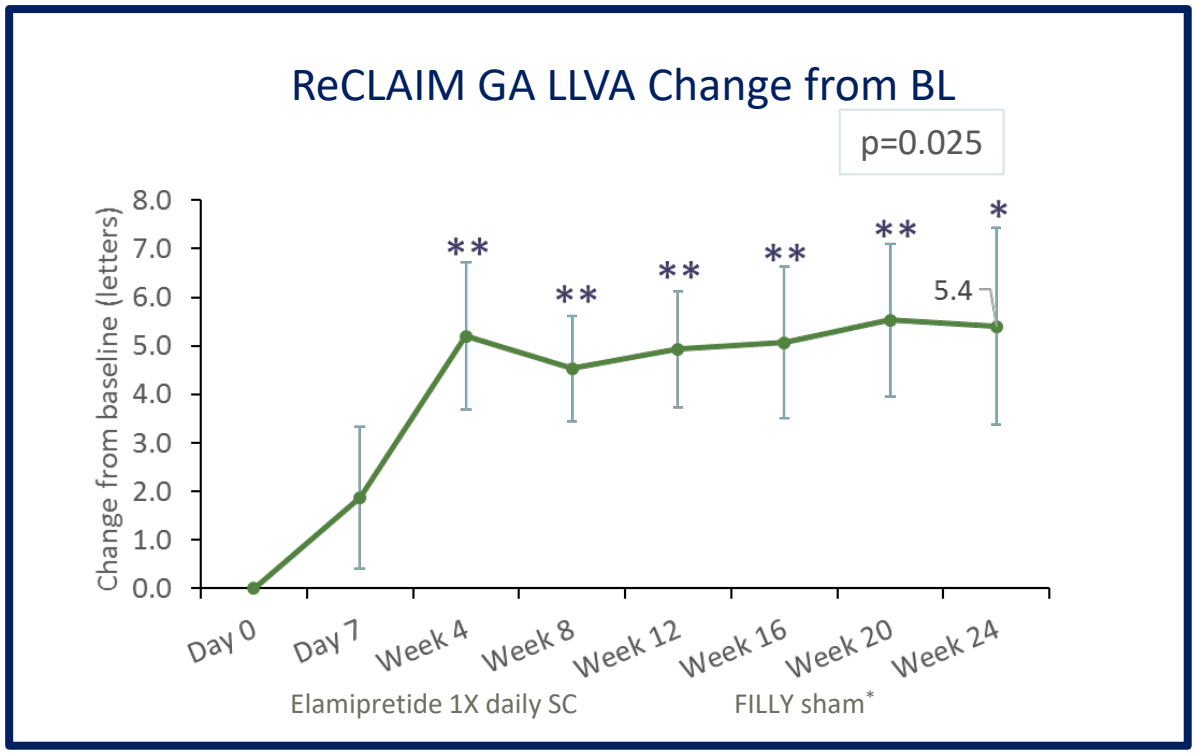
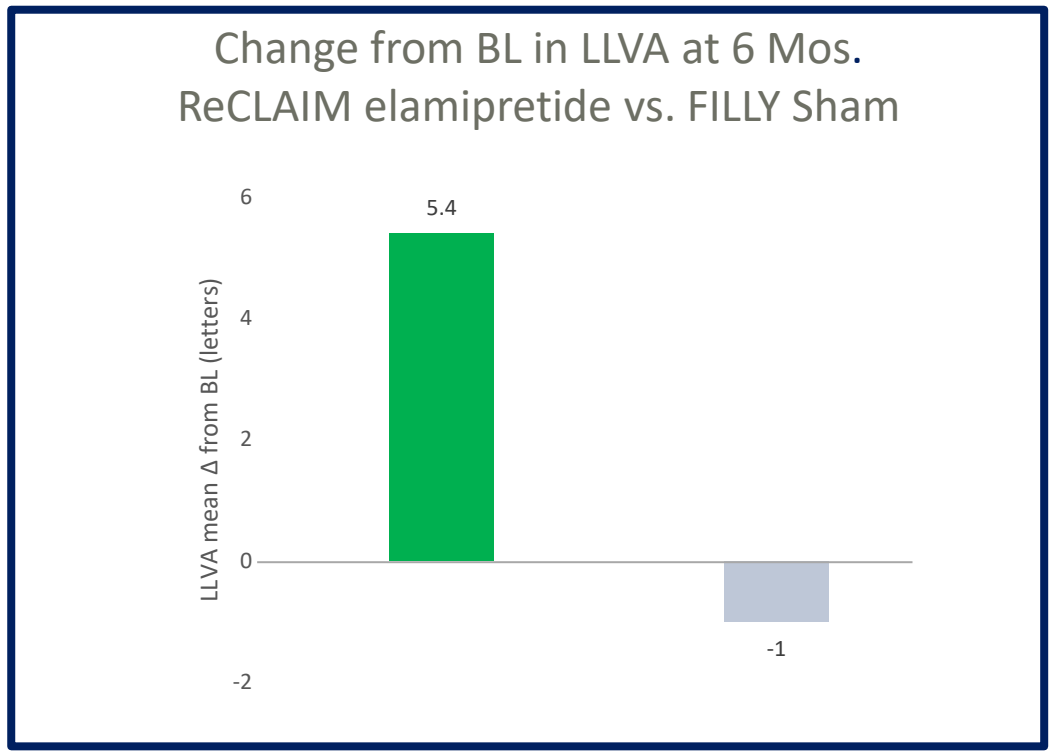
Improved low light visual function in GA





ReCLAIM Phase 1 clinical trial: 40 dAMD patients (19 with GA; 21 with high risk drusen); once daily 40 mg SC elamipretide for 6 months**

- Low light visual acuity (LLVA) improved from BL for drusen (mean +5.63 letters; p=0.006) and **GA patients (mean +5.4 letters; p=0.025)**
- Best corrected visual acuity (BCVA) also improved from BL for drusen (mean +3.4 letters; p=0.04) and **GA patients (mean +4.6 letters; p=0.003)**

*Jaffe et al., Ophthalmology 2020, with 6-month sham LLVA extrapolated from graphic representation
** Mettu et al., Opth Sc Nov 2021; Allingham et al., Opth Sc Dec 2021

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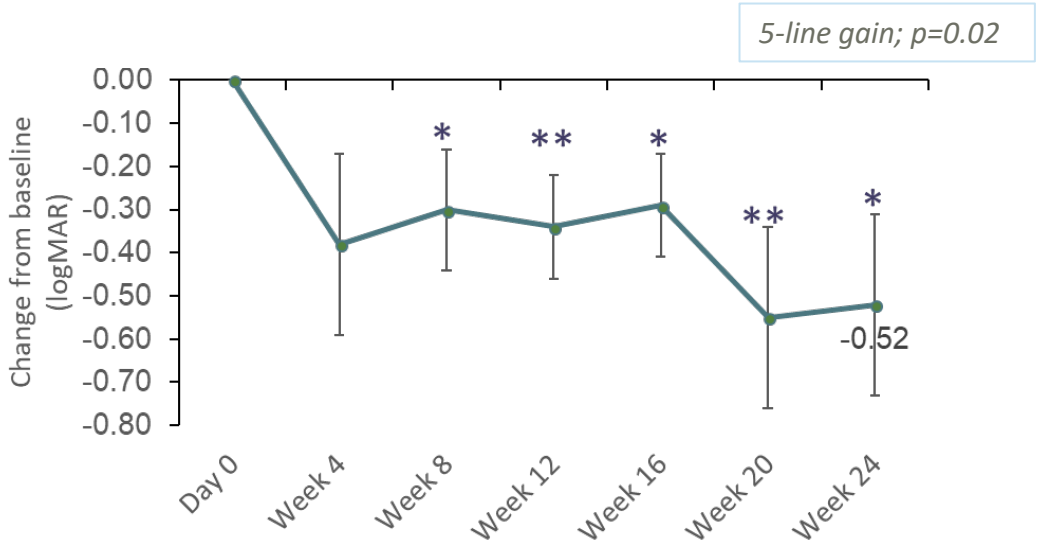
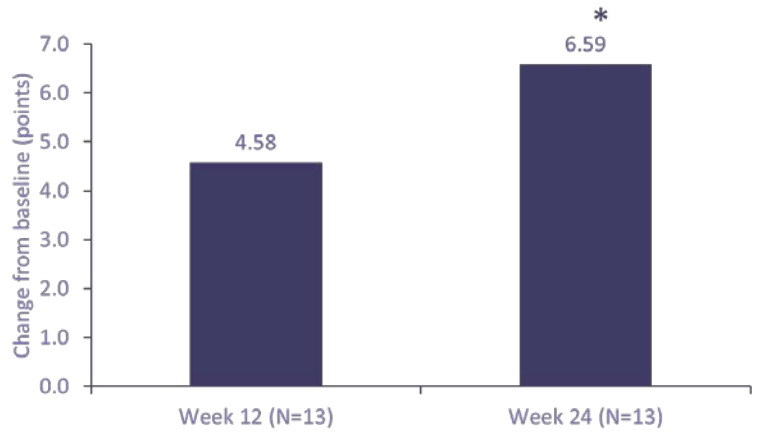
Improved visual quality of life

Mean change from BL in low light smallest line read correctly



Visual Function Questionnaire (VFQ-39)



- Low light reading acuity improved from BL for drusen (mean 3-line gain; p=0.0001) and **GA patients (mean 5-line gain; p=0.02)**
- Visual quality of life on VFQ-39 and low luminance questionnaires improved from BL for GA patients (p<0.05), with clinically significant improvements in peripheral and color vision

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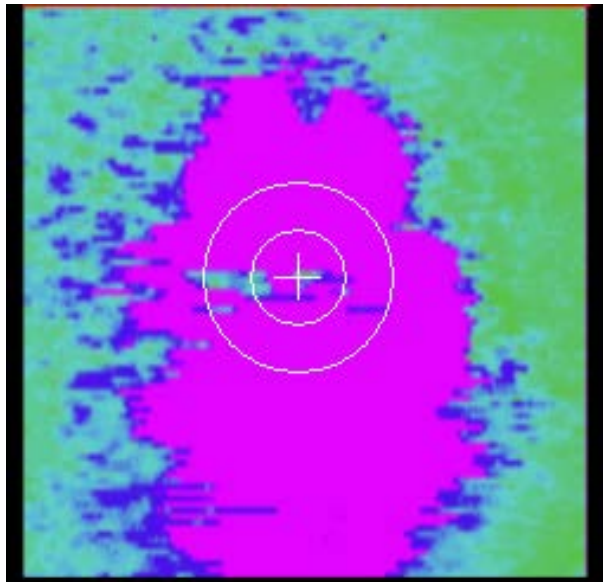
Improved vision correlated with ellipsoid zone health

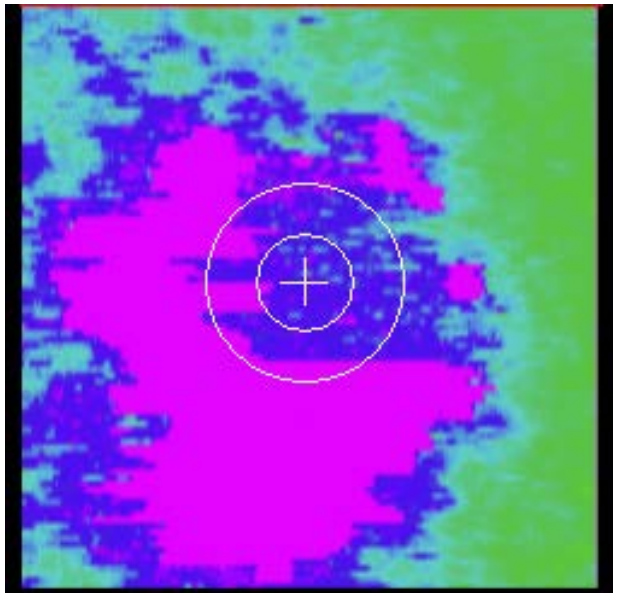
- The ellipsoid zone (EZ) is an area of the retina comprised mostly of mitochondria which supports photoreceptor function and is known to be attenuated in dry AMD
- In a post hoc analysis, ~50% of GA patients gained ≥5 letters in LLVA; with response correlated with baseline macular percentage of total EZ attenuation (r = -0.72; *P* = 0.002)

EZ-zone mapping from illustrative GA patients, w/ indicating attenuation and indicating healthy EZ

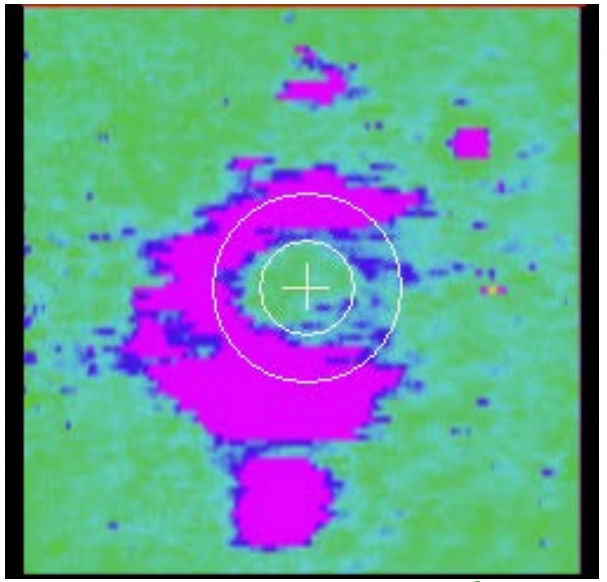
2-letter gain



4-letter gain



18-letter gain



Ehlers et al., ARVO, 2021

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ReCLAIM-2

Topline data expected Q2 2022

Screening	BL	W4	W8	W12	W24	W36	W48	W52: Washout

GA area ≥0.05mm^2/ <10.16 mm^2

BCVA ≥ 55 letters

>5 letters low luminance deficit

n=176

Inclusion criteria mimic Phase 1 ReCLAIM GA cohort (BCVA ≥ 55 letters, >5 letters low luminance deficit)

Elamipretide 40 mg SC or placebo once daily, 2:1 randomization

Efficacy endpoints

Low luminance visual acuity (LLVA)*

Geographic atrophy by optical coherence tomography (OCT)*

Geographic atrophy by fundus autofluorescence (FA)

Low luminance reading acuity (LLRA)

Best corrected visual acuity (BCVA)

NEI Visual Function Questionnaire (VFQ)

Low Luminance Questionnaire (LLQ)

Conversion to choroidal neovascularization (wet AMD)

* Primary endpoint family

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Rare neuromuscular

nuclear Primary Mitochondrial Myopathy (nPMM) ~7,000*

- *Fast track + orphan drug designation*

Duchenne muscular dystrophy (DMD) 12,000 – 15,000

* All estimates are of US patients affected

Mitochondrial ATP production is critical for skeletal muscle function. During movement, the rate of energy used by skeletal muscles increases exponentially, e.g., >100-fold increase almost instantly during strenuous exercise. Mitochondria play an essential role in sustaining cellular energy levels to match energy demand.

Defects in energy metabolism lead to muscle dysfunction in age-related diseases and in rare genetic diseases such as primary mitochondrial myopathy (PMM) and Duchenne Muscular Dystrophy (DMD).

Glancy et al., Nature, 2015; Park et al., Am J Physiol Heart Circ Physiol. 2014

nPMM Key Advisers: Lawrence Bindoff, MD, PhD; Bruce Cohen, MD, FAAN; Thomas Klopstock, MD, FEAN; Mary Kay Koenig, MD; Michio Hirano, M.D., Amel Kara, MD; Michelangelo Mancuso, MD, PhD; Johan van Hove, MD, PhD

DMD Steering Committee: Linda Cripe, MD; Gerassimos Fillipatos, M.D.; Pat Furlong; Kan Hor, MD; Beth McNally, MD; Lee Sweeney, PhD; Jim Udelson, MD; Chet Villa, MD

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nDNA-related primary mitochondrial myopathy (nPMM)

"[My son] is 11 now but has the functional abilities of a toddler. His mobility is limited, and he primarily uses a wheelchair to get around. His life is not easy, but he is a fighter and my personal hero. He is an inspiration and brings so much joy to my life and to so many others.

UMDF Voice of the Patient Report, 2019.

debilitating muscle weakness

exercise intolerance + peripheral neuropathy

most common

mitochondrial genetic mutation (POLG)

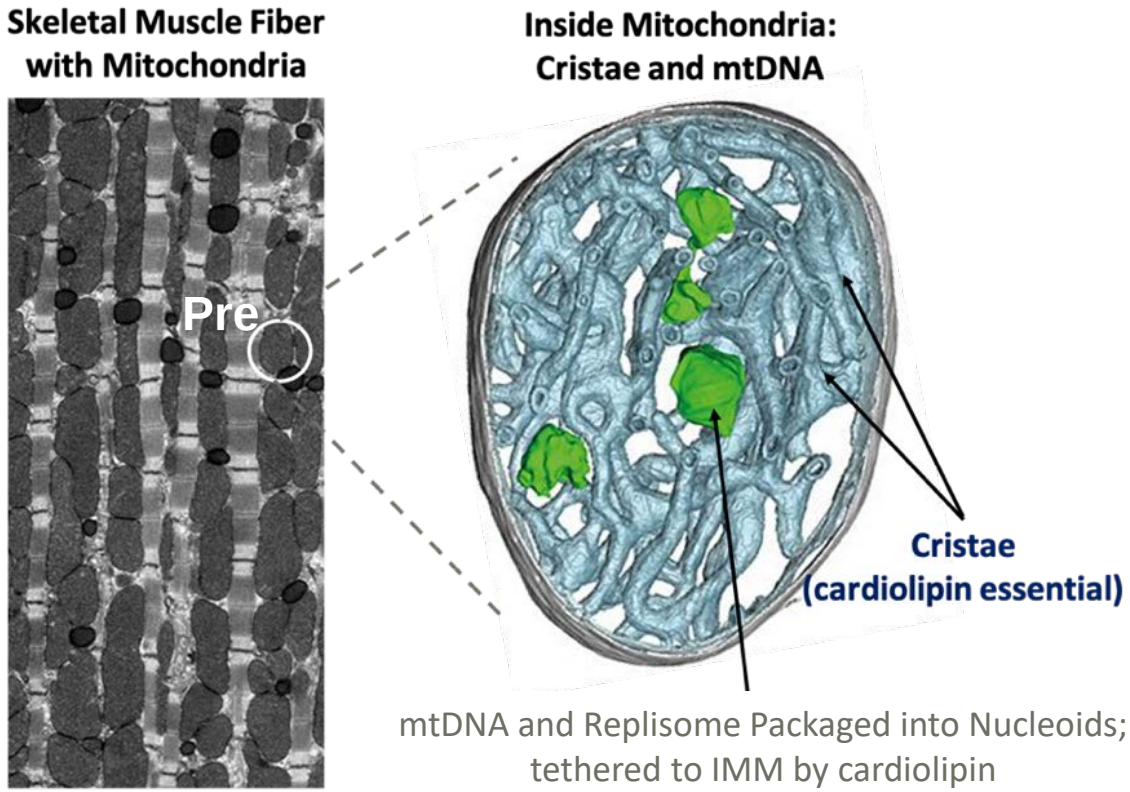
also involves mutations in TWNK, SSBP, MGME1, RNASEH1, DNA2, MVP17, TYMP, DGUOK, RRM2B, SLC25A4, TR2, SUCLG1, SUCLA2

<7,000

patients in the United States

nDNA-encoded mitochondrial replisome replicates mtDNA

to meet skeletal muscle energy demands



mtDNA and Replisome Packaged into Nucleoids; tethered to IMM by cardiolipin

Modified from Glancy et al., 2017; Kukat et al., PNAS 2015

Cardiolipin is required for nuclear protein importation, replisome tethering, and mitochondrial dynamics

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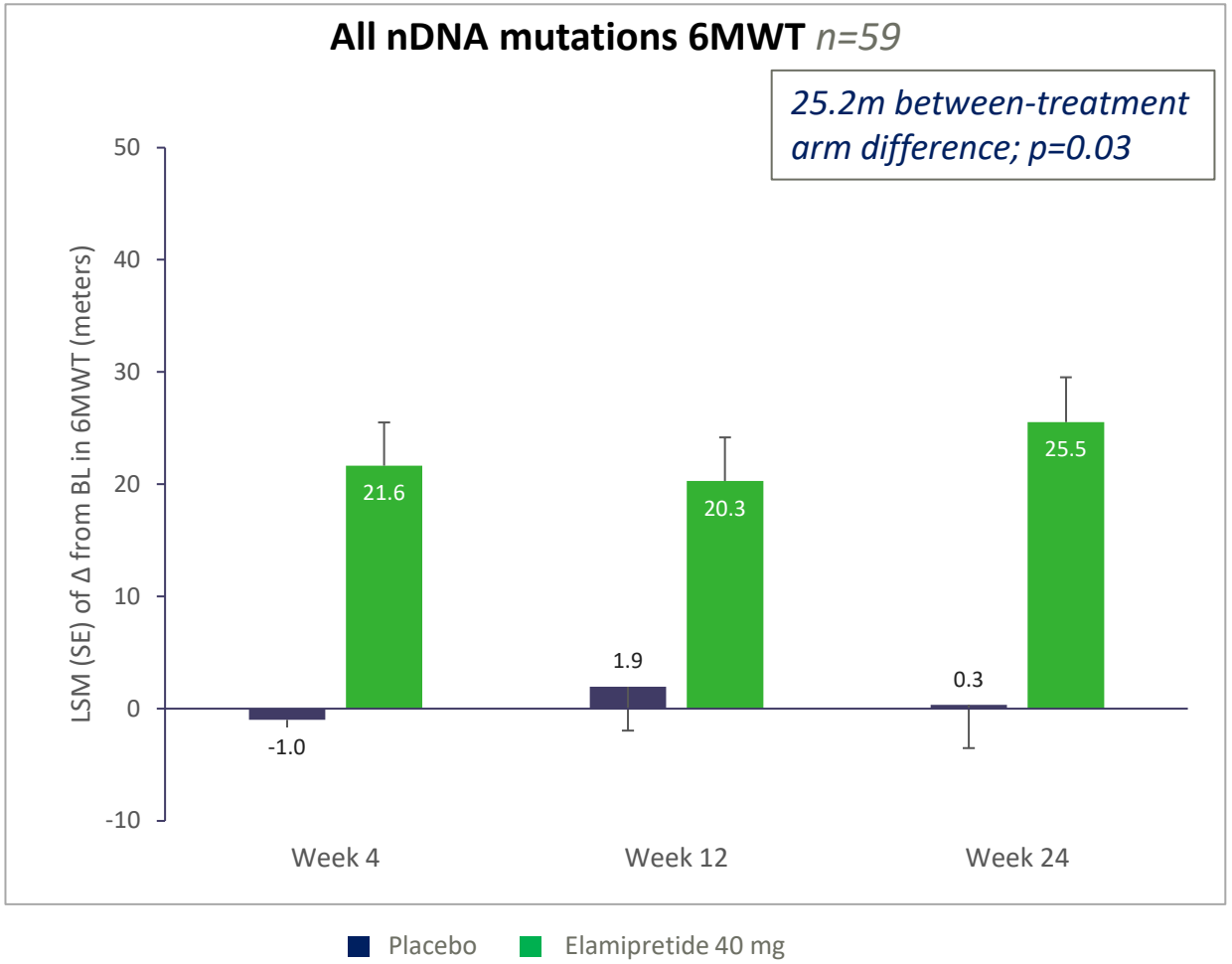
Prespecified nPMM subgroup improved in MMPOWER-3



Improvements observed in MMPOWER-3 nDNA subgroup

- MMPOWER-3 enrolled 218 patients with PMM due to mtDNA (~75%) and nDNA (~25%) mutations. Primary endpoints were not met across the full intent-to-treat patient population, which was attributed primarily to heterogeneity of disease presentation across different groups of genetic mutations.
- Pre-specified stratification enabled subgroup analysis of nDNA versus mtDNA patients, demonstrating that nDNA patients (n=59) improved on 6MWT.
- The increase in walk distance for subjects with an nDNA mutation was a function of elamipretide drug exposure (p = 0.03).

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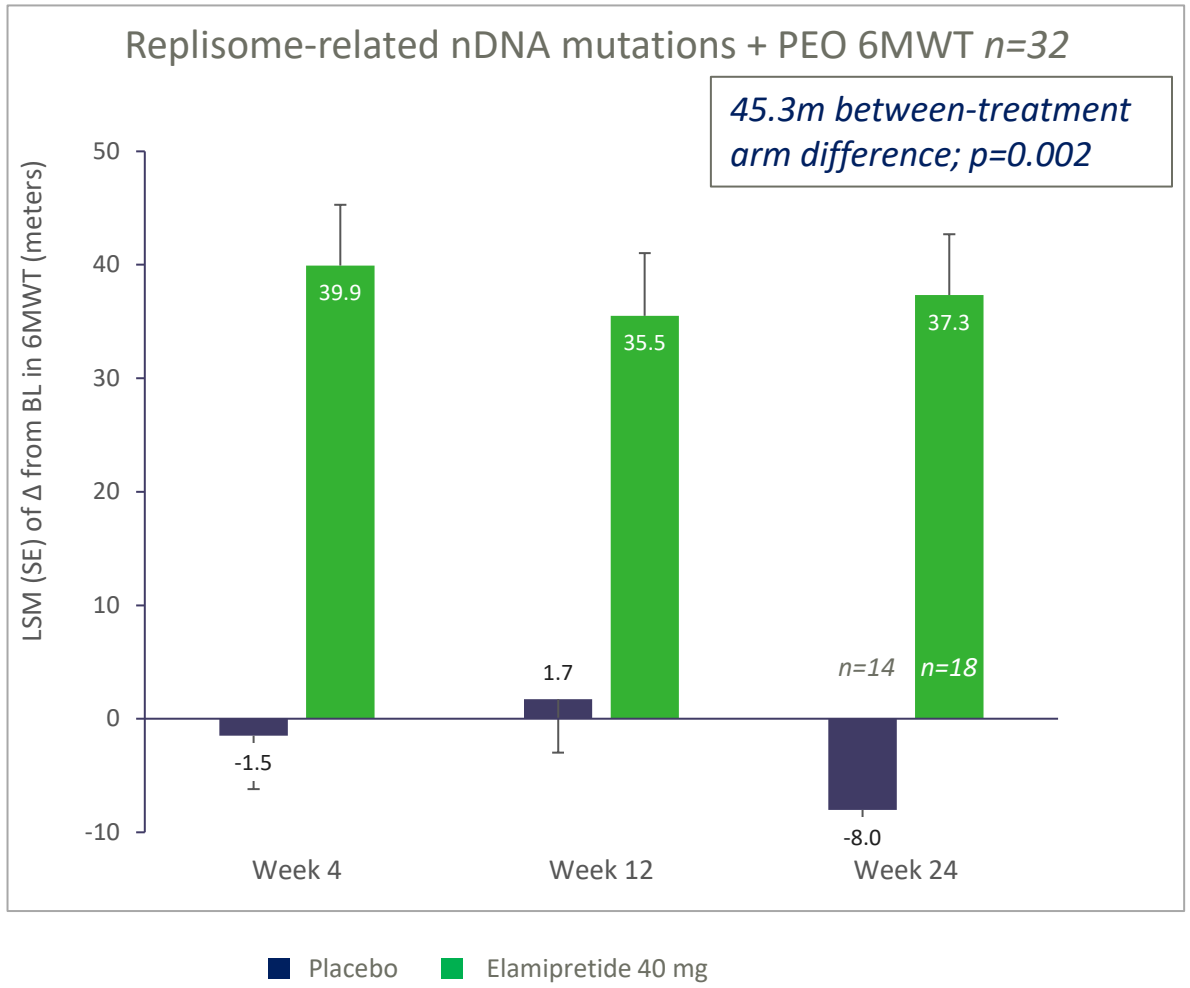
nPMM clinical data suggested P3 enrichment strategy

Post-hoc analysis of nPMM patients meeting NUPOWER inclusion criteria



Enriching for replisome-related nDNA mutations + PEO ensures myopathic phenotype, predicts more robust response

- Primary mitochondrial disease, including due to replisome-related nDNA mutations, can affect multiple organ systems. Ensuring a homogeneous clinical disease presentation is key to clinical trial design.
- Patients with a primarily myopathic disease typically experience ocular muscle involvement, characterized by progressive external ophthalmoplegia. External thought-leaders suggested enriching for this co-morbidity to reduce heterogeneity.
- A post-hoc analysis of the MMPOWER-3 data supports enriching for patients with replisome-related nPMM who have signs and symptoms of PEO.

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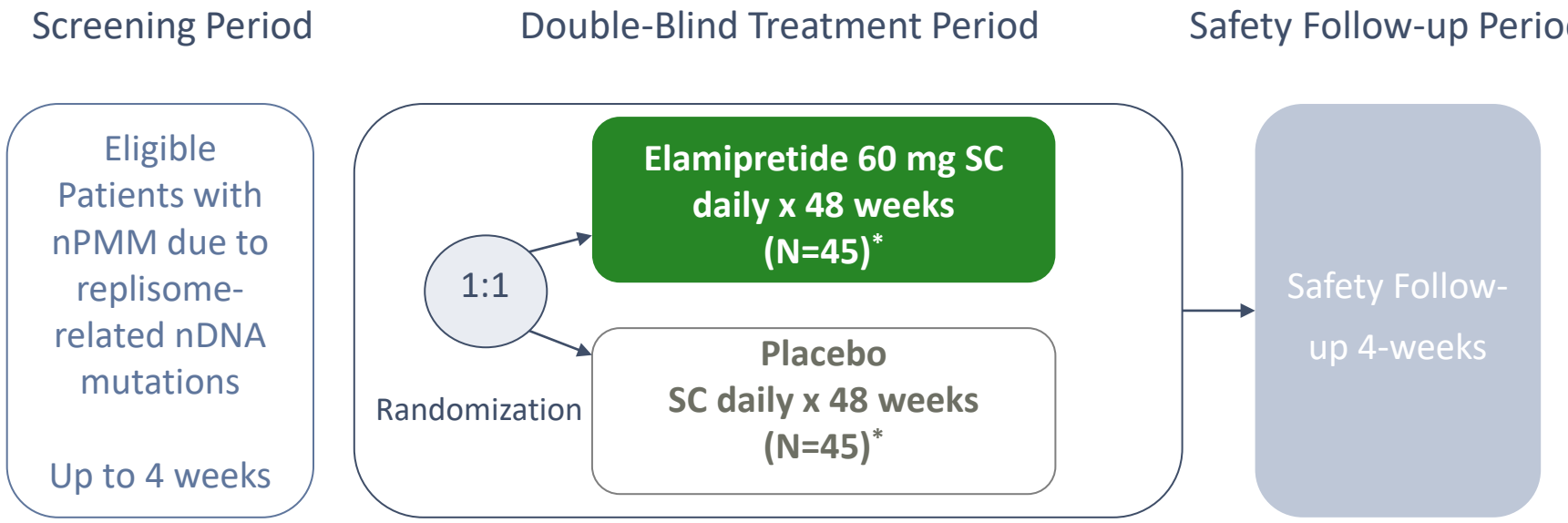
nPMM Phase 3 trial design

NuPOWER Phase 3 Clinical Trial



* Up to 40 additional patients with nPMM due to non-replisome nDNA mutations

- Primary efficacy analysis in patients with POLG and other replisome-related mutations (n=90)
- 60 mg SC once-daily
- 6MWT primary endpoint; 5XSST, 3TUG, PROs secondary endpoints
- 1-year duration
- P3 patient recruitment ongoing.

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Duchenne's muscular dystrophy

Pressing unmet need in cardiomyopathy

"Heart issues don't just affect some people with Duchenne; they affect ALL people with Duchenne. While advances in respiratory care have improved respiratory outcomes, heart muscle disease…and heart failure remain the leading cause of death in Duchenne." www.parentprojectmd.org/why-the-heart-matters

virtually all

develop cardiomyopathy by age 18

heart failure

is a leading cause of death

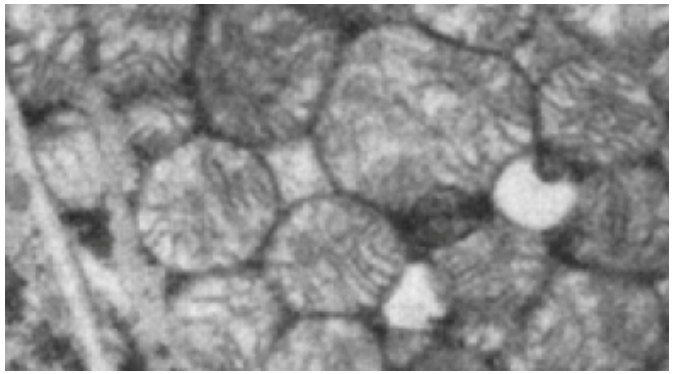
19.6

average age of death for patients with cardiomyopathy

Meyers, Townsend, Int J Mol Sci. 2019; Nigro, Acta Myol. 2012; Payne, R.M., Prog. Pediatr. Cardiol., 2011; Giugliano, GR et al., Tex Heart Inst J, 2007; Machiraju et al., Front Cardiovasc Med 2019.

Targeting alternative therapeutic pathways for cardiomyopathic and neuromuscular disease

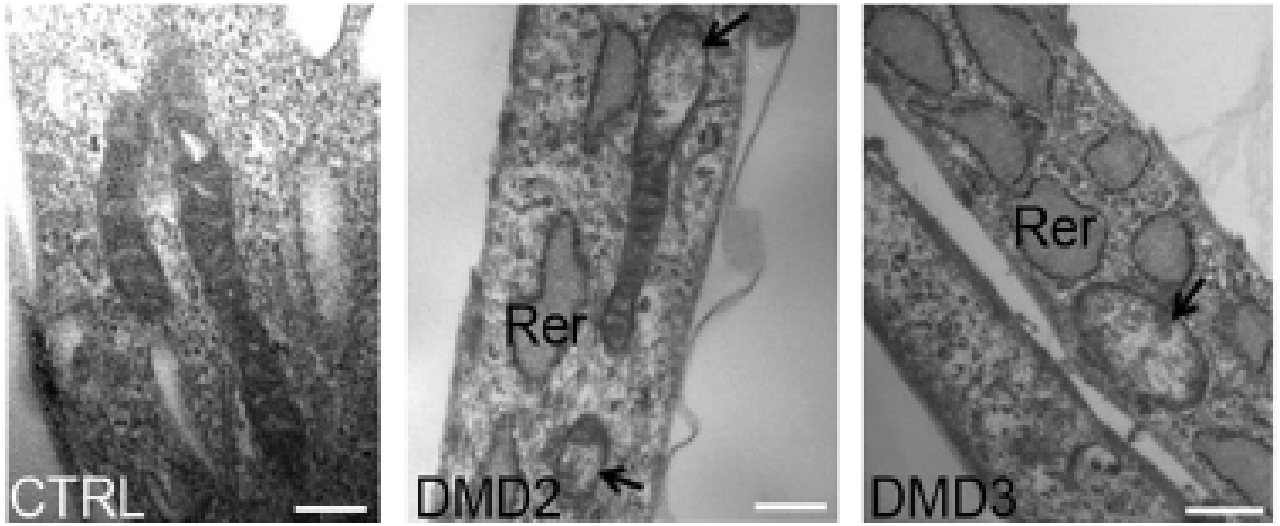
Electron microscopy of biopsied cardiac muscle in 6-year-old boy with DMD, EF 58



May compliment approved therapeutic class:

- In DMD, impaired energetics is observed *before* declines in muscle function across species
- "Mitochondrial energy production is limited early in the disease process, *well before significant fibrosis or declines in contractile function are evident*."

Ultrastructural analysis of normal and DMD myoblasts (reduced matrix density; swelling).



Wakai et al., 1988; Pellegrini et al., 2013; Meyers and Townsend, Int J Mol Sci 2019

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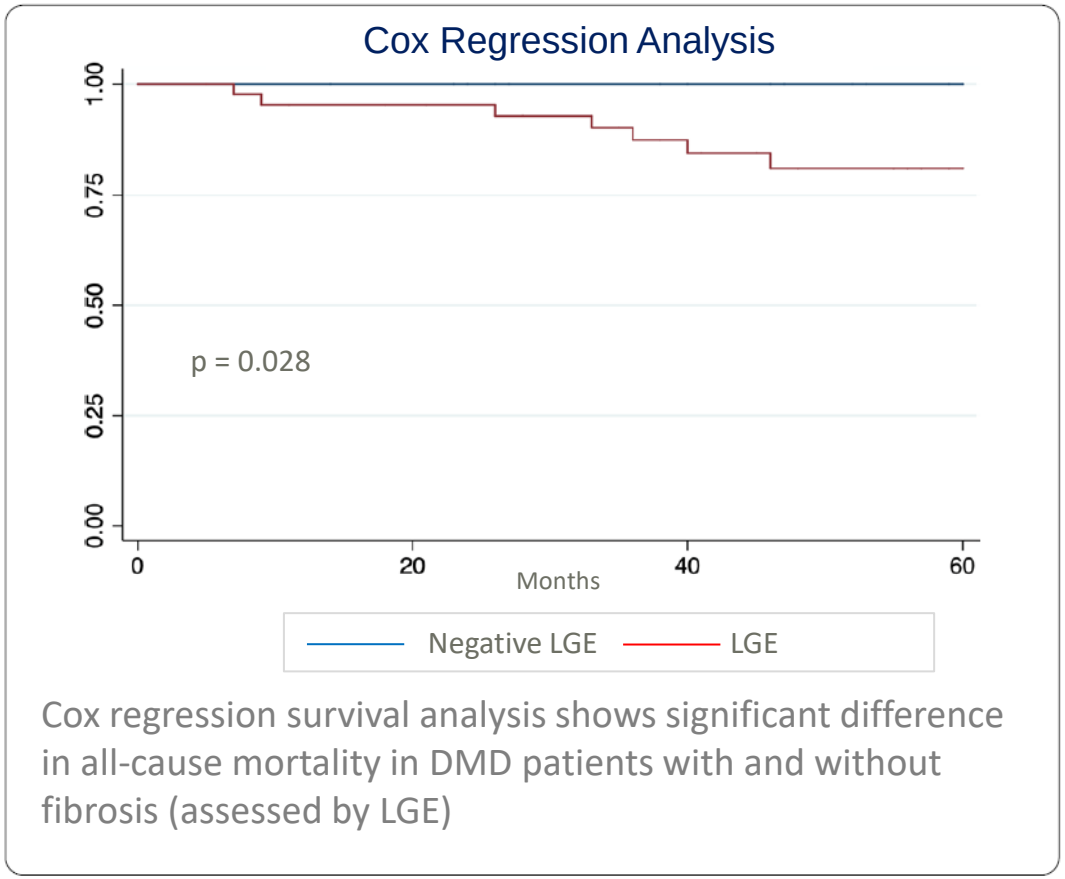
Stealth BIOTHERAPEUTICS

DMD cardiomyopathy

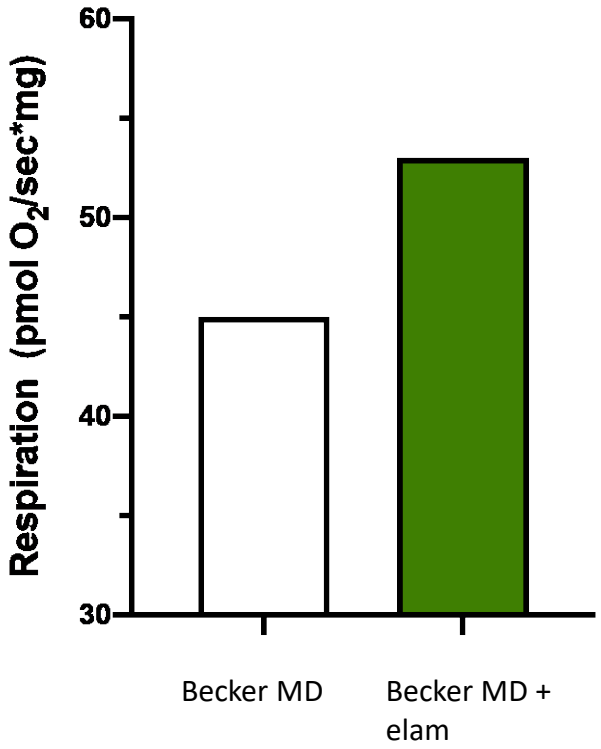
✓ Fibrosis is associated with poor outcomes in DMD



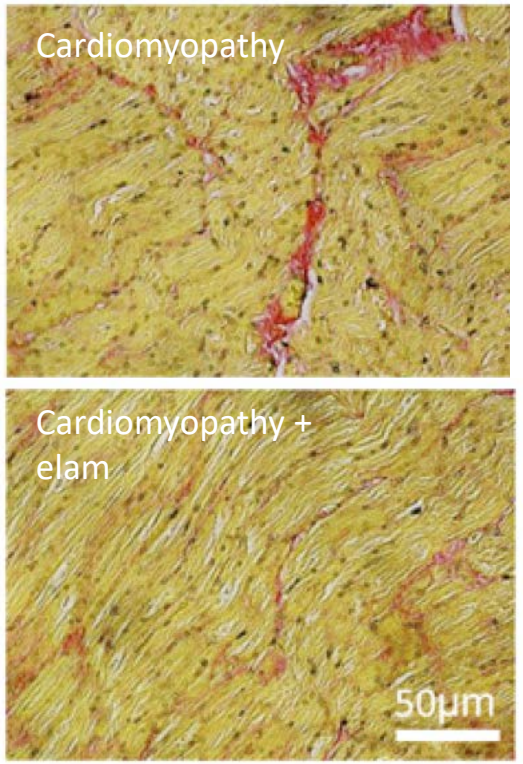
Cox regression survival analysis shows significant difference in all-cause mortality in DMD patients with and without fibrosis (assessed by LGE)

Raucci et al., J Cardiovasc Magn Reson, 2021.

Elam improves mitochondrial respiration in a dystrophic human heart



Elam improves fibrosis in non-ischemic cardiomyopathy (HFpEF model)



Red = fibrotic tissue

Stauffer, unpublished, 2020; Hughes, 2019; Eirin et al., JAHA 2016

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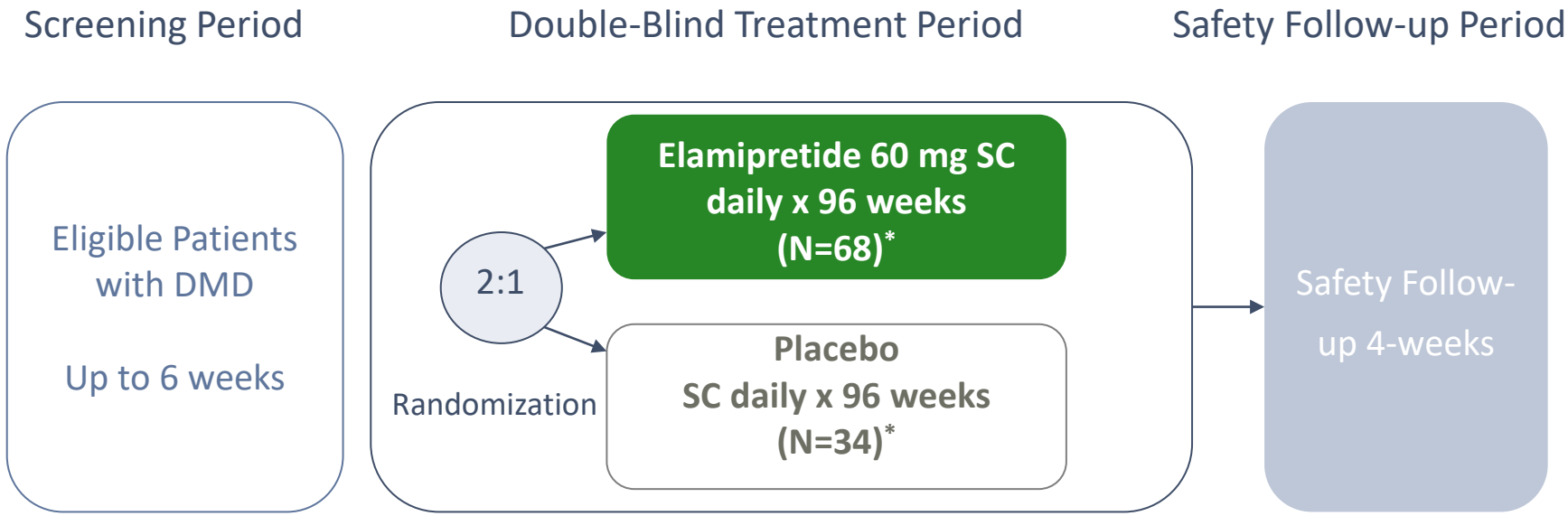
DMD proposed clinical plan*



Primary endpoint:

LGE (grams of fibrosis) assessed by cardiac magnetic resonance imaging

Secondary/exploratory endpoints:

global circumferential strain, left ventricular stroke volume, left ventricular ejection fraction, forced vital capacity, patient reported outcome assessments.

* Natural history review ongoing and IND submission planned following positive pre-IND meeting

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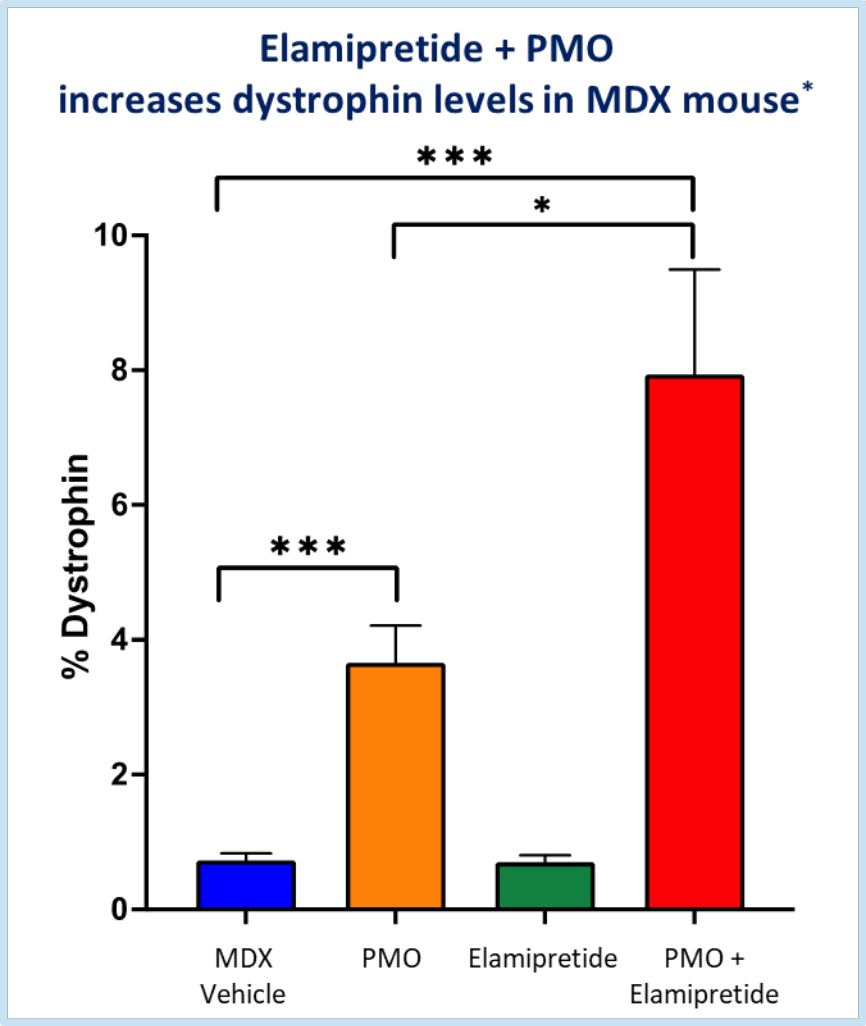
Targeting dystrophin in DMD

Therapeutic Approaches in DMD

- ✓ Across multiple preclinical models, elamipretide has been shown to improve mitochondrial structure and function and
  - ✓ Decrease fibrosis and inflammation
  - ✓ Blunt loss of muscle mass and increase regeneration
  - ✓ Correct aberrant cellular calcium handling
  - ✓ Correct blood flow regulation
- ➢ Replace dystrophin/increase utrophin



* *Preliminary data; final report pending.*

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Rare cardiology

Barth syndrome <200

- *Fast track + orphan drug + rare pediatric designation*

Mitochondria in the healthy heart produce 95% of the approximately 6 kg of adenosine triphosphate (ATP) utilized daily to pump blood through the body.

Mitochondria comprise ~35% of the volume of cardiomyocytes, the primary contractile cells in the myocardium.

Decrements in mitochondrial energy homeostasis trigger numerous responses in gene expression, lead to vicious cycles of damage-mediated signaling, and promote overall remodeling of the heart (dilation, hypertrophy) over time.

Dudek and Maack, 2016; Martinez et al. 2017; Sabbah, 2020.

Key Advisers: *Javed Butler, M.D., Brian Feingold, MD; John Jefferies, MD; Kan Hor, MD; Tony Sabbah, PhD; Carolyn Taylor, MD; Reed Thompson, M.D.; Jeffrey Towbin, MD; Jim Udelson, MD; Hilary Vernon, M.D., PhD; Gerard Vockley, M.D.*

All estimates are of US patients affected; BSF Voice of the Patient Report, 2019; Hanson, et.al., World J Cardiol., Jan. 2019; Payne, R.M., Prog. Pediatr. Cardiol., 2011; Giugliano, GR et al., Tex Heart Inst J, 2007; Machiraju et al., Front Cardiovasc Med 2019; Vasan et al., JACC: Cardiovascular Imaging 2018; Sabbah HN. Heart Fail Rev. 2020 Oct 1.

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Barth syndrome

"On April 23rd in 2000, I suffered my first cardiac arrest at age 11, and I had my first defibrillator implanted. On April 17th, 2018, I suffered my eighth cardiac arrest and was saved by the shock of my fourth defibrillator."

- BTHS Voice of the Patient Report

cardiolipin deficit
caused by genetic defect

<200
diagnosed

90% report
cardiomyopathic symptoms

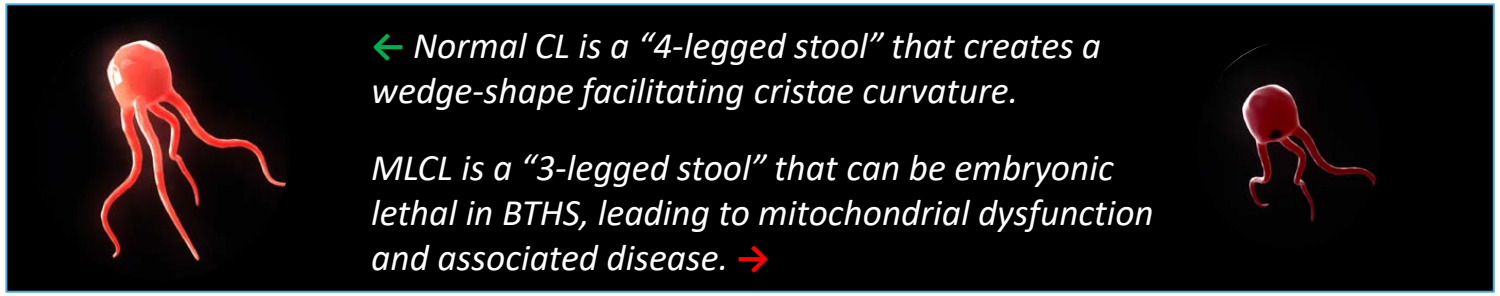
85% mortality
by age 5

Barth Syndrome Foundation Voice of the Patient Report, 2019; PFDD Conference, 2018; BSF website Elamipretide Petition Resources.

Patient-centric drug development:

a cardiolipin-targeted drug for a lethal disease of cardiolipin deficiency

- In Barth syndrome (BTHS), pathogenic mutations in the *TAZ* gene lead to 70-95% deficits in normal cardiolipin (CL). Instead, patients have elevated levels of a variant called monolysolcardiolipin (MLCL). The disease can be embryonic lethal, and in all known cases has led to premature death.



- In 2014, patient advocacy and Johns Hopkins, the only multi-disciplinary center treating BTHS in the U.S., requested that elamipretide be assessed for BTHS, prompting development efforts.

- Elamipretide has been assessed in a Phase 2 clinical trial and open label extension and a Phase 3 retrospective natural history control trial. Regulatory discussions are ongoing to determine future development activities.

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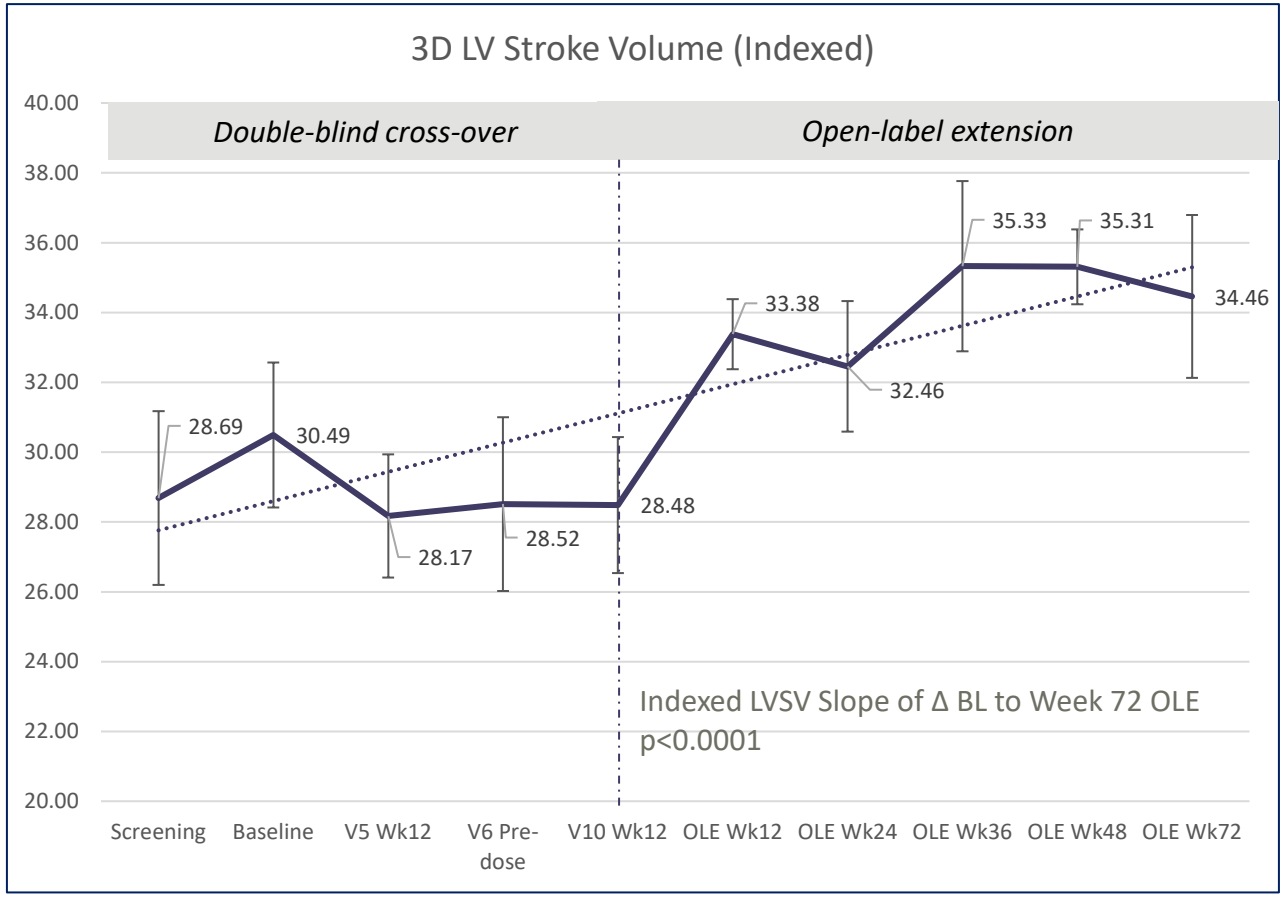
Long term data suggests reversal of disease pathology

BTHS patients had severely impaired left ventricular (LV) function with low LV end diastolic, end systolic, and stroke volume.



Indexed LVEDV slope of Δ BL to Week 72 OLE p<0.0001
Indexed LVESV slope of Δ BL to Week 72 OLE p=0.0002

- **Stroke volume** (SV) is an important indicator of how efficiently the heart can meet the body's demand for perfusion to various organs.
- **Correlations between improvements in SV and functional endpoints** (6MWT) strengthened with long-term OLE therapy (OLE Week 72 r=0.52).
- Changes in cardiac function and structure may suggest **durable reversal of disease pathology**.
- The ratio of abnormal to normal cardiolipin, which is diagnostic for the disease, also improved over time (OLE Week 72, p=0.03)

SV: the amount of blood pumped by the heart's left ventricle per contraction and a primary determinant of cardiac output (CO).

CO: the volume of blood pumped by the heart.

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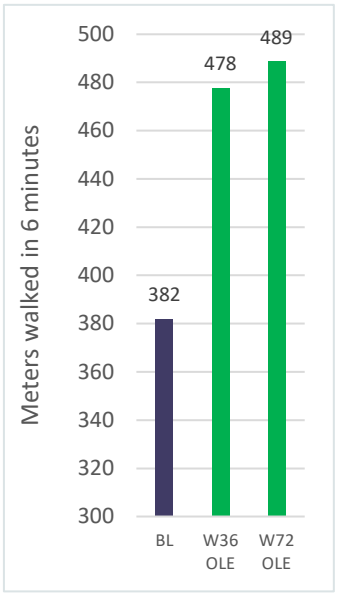
Long term efficacy during OLE

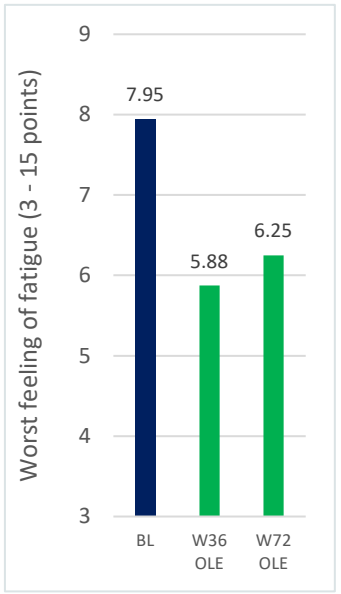
>100-meter improvement in 6MWT, durable >2 years, exceeds reported effects of other drugs in HF trials.[1]

6MWT (n=8)



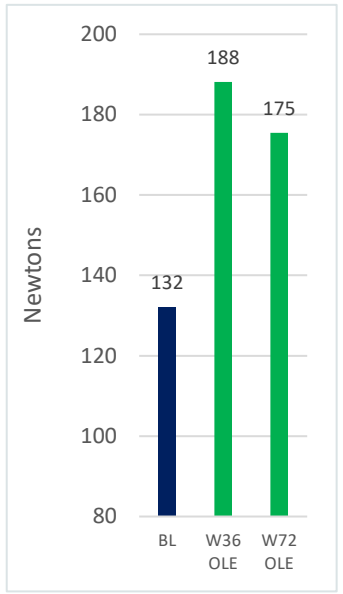
Wk 36 OLE p=0.02
Wk 72 OLE p=0.01

BTHS-SA fatigue (n=8)



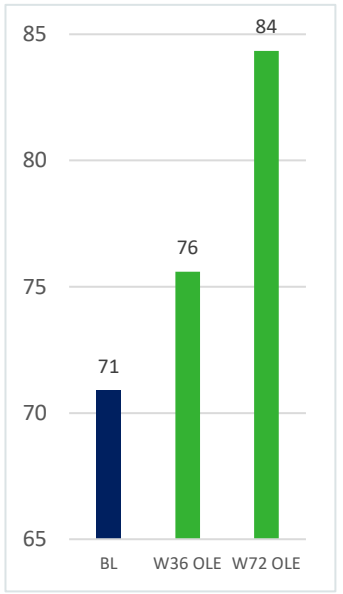
Wk 36 OLE p=0.03
Wk 72 OLE p=0.07

Muscle strength (n=8)



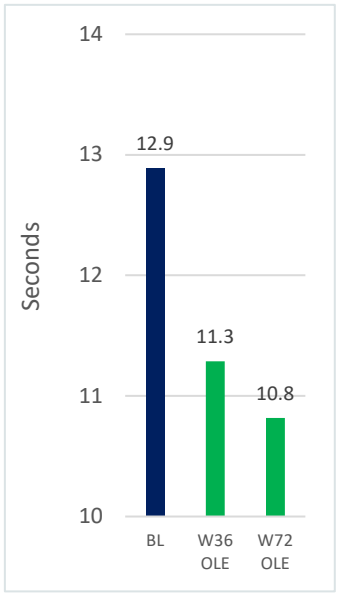
Wk 36 OLE p=0.02
Wk 72 OLE p=0.008

SWAY balance (n=8)



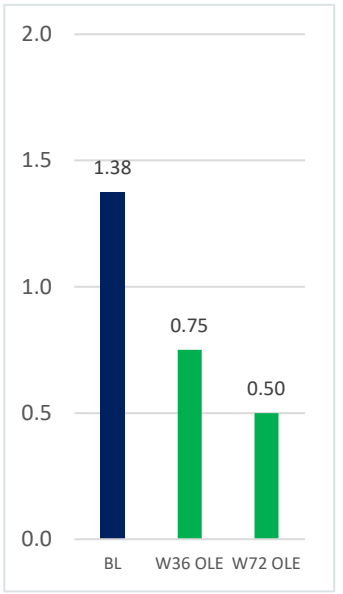
Wk 36 OLE p=0.20
Wk 72 OLE p=0.01

5X SST (n=8)



Wk 36 OLE p=0.22
Wk 72 OLE p=0.10

CGI Symptoms (n=8)



Wk 36 OLE p=0.10
Wk 72 OLE p=0.0006

- **Borg scale:** no observed increase in effort from Part 1 baseline through OLE Week 72, suggesting that improvement was not due to expectational bias.

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[1] Olsson, Lars et al., European Heart Journal (2005) 26, 778–793 doi:10.1093/eurheartj/ehi162

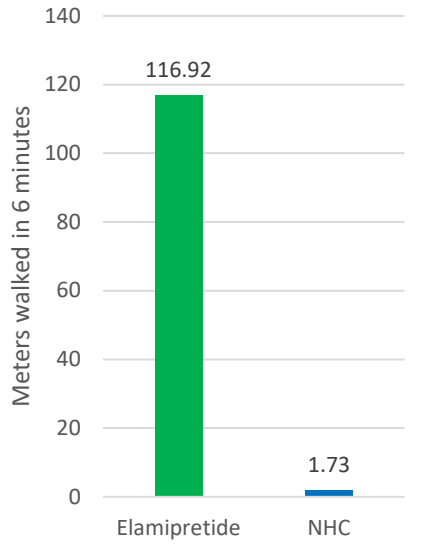
Stealth BIOTHERAPEUTICS

SPIBA-001 Phase 3 met primary endpoint

*TAZ*POWER Week 72 OLE compared to prognostically matched natural history controls (NHC)*

Primary endpoint

6MWT Δ from baseline

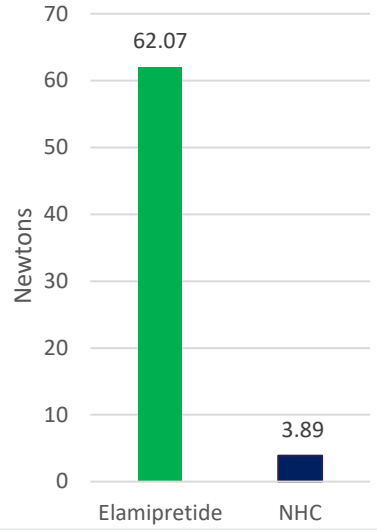


Week 72 OLE: p=0.0003

Week 36 OLE: Elam 80.30, NHC 0.60, p=0.0004
Week 48 OLE: Elam 91.86, NHC 0.89, p=0.0005

Secondary endpoints

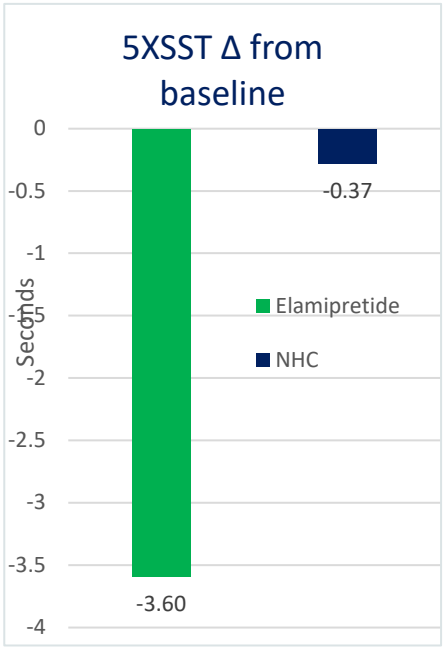
Muscle strength by HHD Δ from baseline



Week 72 OLE: p=0.0002

Week 36 OLE: Elam 41.79, NHC 1.04, p=0.0002
Week 48 OLE: Elam Δ 48.67, NHC Δ 1.97, p=0.0005

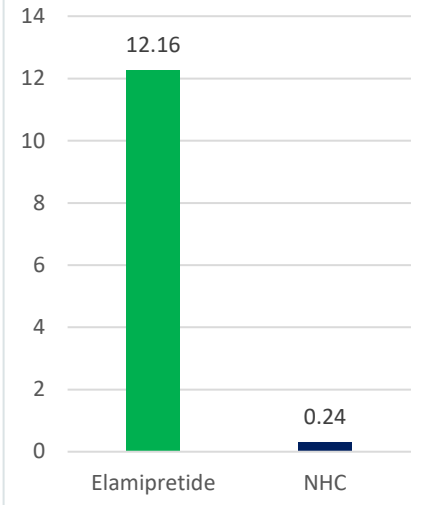
5XSST Δ from baseline



Week 72 OLE: p=0.008

Week 36 OLE: Elam -2.36, NHC -0.002, p=0.042
Week 48 OLE: Elam Δ -2.83, NHC Δ -0.003, p=0.034

SWAY balance Δ from baseline

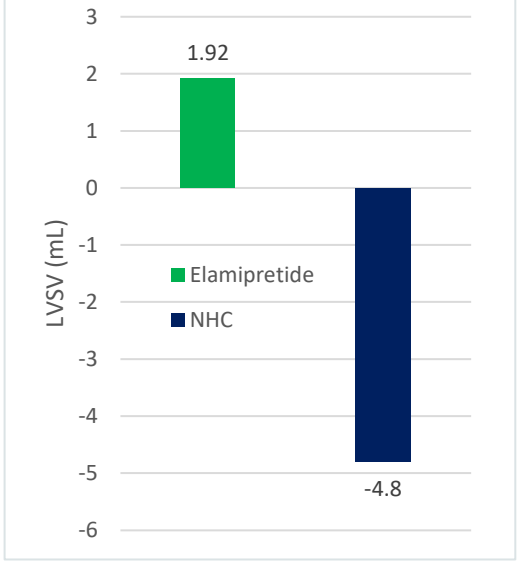


Week 72 OLE: p=0.03

Week 36 OLE: Elam 7.40, NHC 0.86, p=0.13
Week 48 OLE: Elam 8.81, NHC 1.08, p=0.12

Cardiac function

LVSV Δ from BL



Week 72 OLE: LSM 6.72, p=0.002

*Week 72 analysis conducted post-hoc at FDA request

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Thompson WR, et al., *J Cardiac Failure*. October 1, 2020; 26(10);S67. Abstract # 187; Thompson, R., et al, Genet Med. 2020 Oct 20. .

Rare neurology

SBT-272 and pipeline

ALS, FTD and other indications being explored preclinically

The brain accounts for about 2% of our body weight and consumes about 20% of our total oxygen and about 25% of our total energy supply.

100s-1,000s of mitochondria are contained in a single neuron.

Neurons depend almost entirely on mitochondrial oxidative phosphorylation for their energy supply.

Mitochondrial dysfunction has been implicated in diseases such as Parkinson's, Alzheimer's and Huntington's diseases and amyotrophic lateral sclerosis (ALS) as well as in genetic mitochondrial diseases.

Wong-Riley, Eye Brain, 2010; Rango, et. al., Genes, 2018..

* All estimates are of US patients affected

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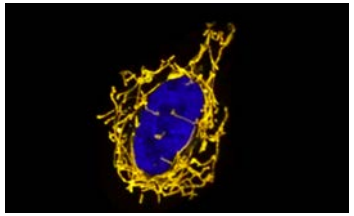
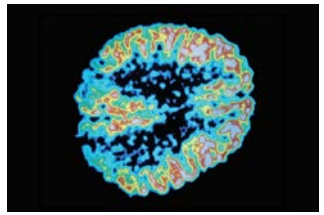
SBT-272 is a novel neuroprotective agent

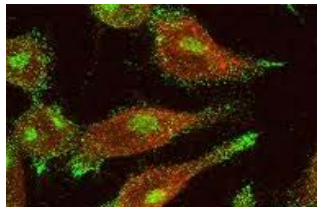


Mitoprotection

Neuroprotection



Brain metabolism



↓ protein aggregates

↓ motor deficit

↓ inflammation

	Mitoprotection	Neuroprotection	Brain metabolism	↓ protein aggregates	↓ motor deficit	↓ inflammation
Amyotrophic lateral sclerosis	✓ TDP-43	✓ TDP-43			✓ SOD-1	
Frontotemporal dementia	✓	✓		✓		
Alpha-synucleinopathy	✓	✓		✓		✓
Huntington's disease*	✓		✓		✓	
Cerebral ischemia reperfusion	✓					

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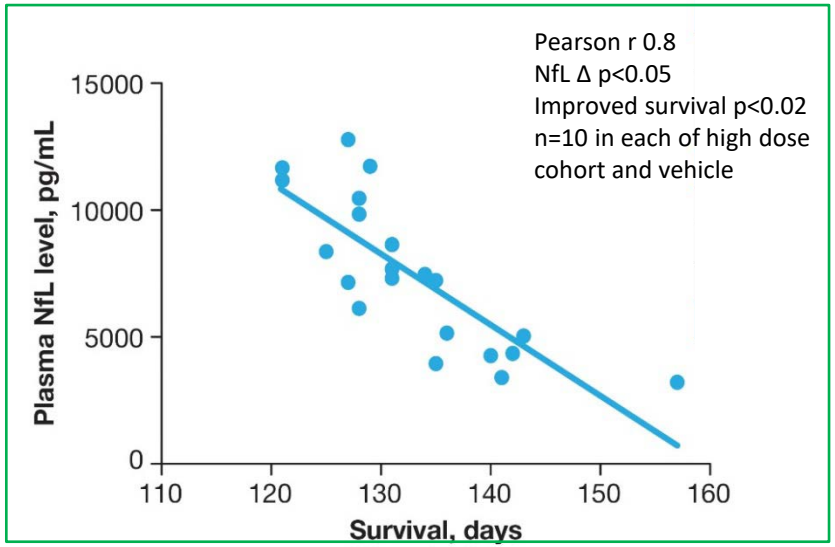
* Directional signal for mito-protection; neurotransmission biomarkers improved; some behavioral modifications

Stealth BIOTHERAPEUTICS

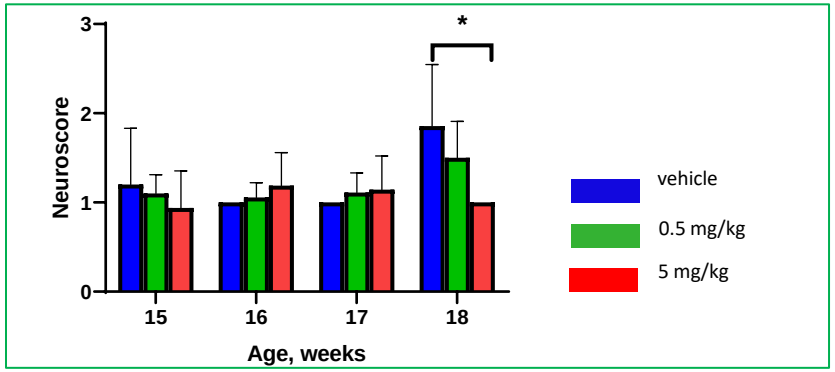
SBT-272 in ALS models

Improved survival, NfL, motor function in ALS SOD-1 model

Male survival correlated with improvement in neurofilament light chain (NfL).

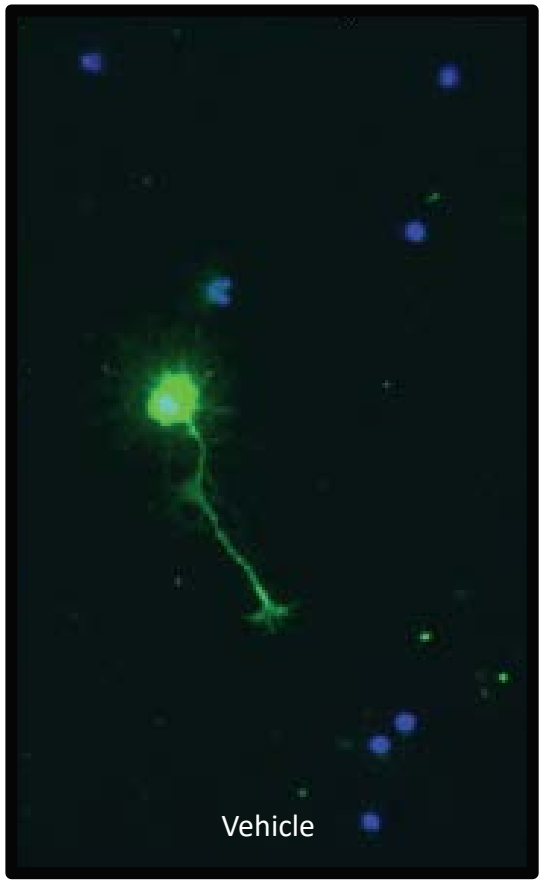


Dose-dependent improvement in motor function (Neuroscore) in males

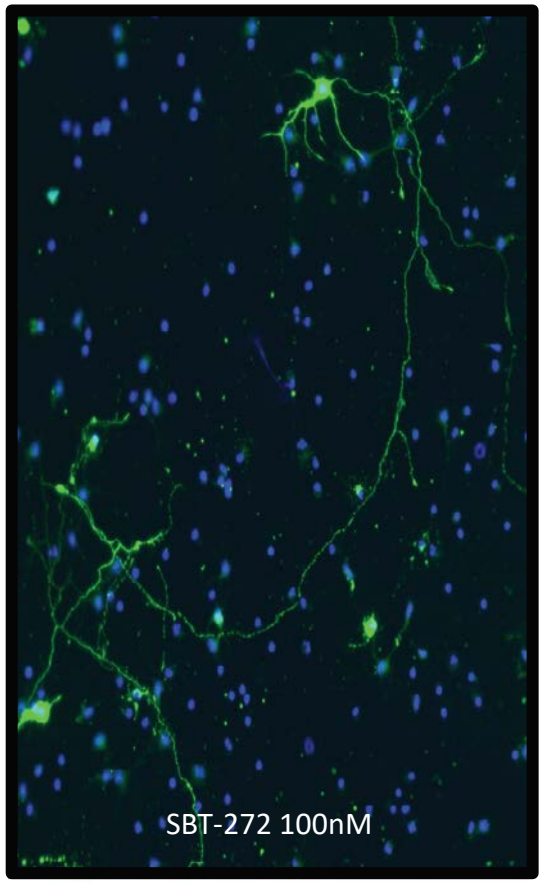


Mito-protection and neuroprotection in ALS TDP-43 model

Improved neurite length and branching in mutant TDP43 primary upper motor neurons



Short axon; large growth cones, disintegrating axons



Improved morphology and health, long axons, networking with branch points and arborizations

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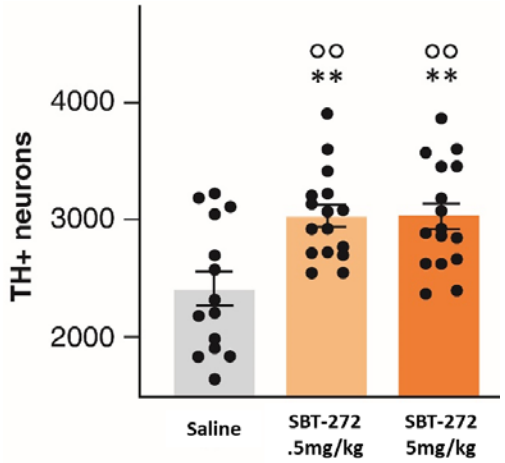
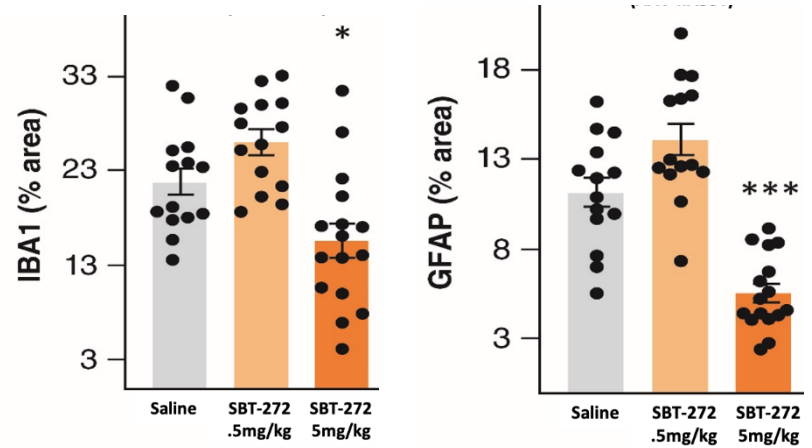
SBT-272 in dementia models

Neuroprotection, reduced protein aggregates and inflammation in *α-Syn* model

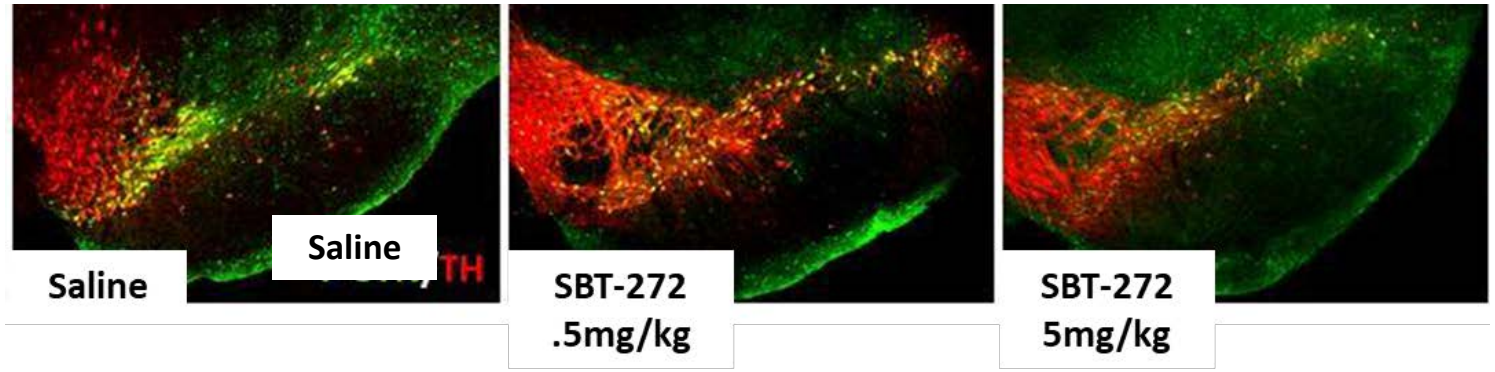
Reduced Loss of Dopaminergic Neurons

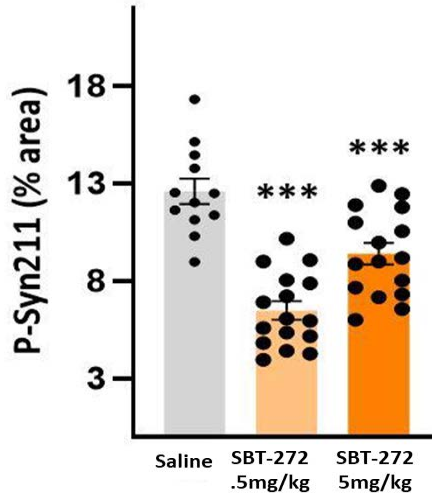


Dose-dependent Reduction of Inflammation



Improved Clearance of α-Syn Protein Aggregates





**p<0.01 vs A; ***p<0.001 vs A; °°p<0.01 vs C1-C2

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Pipeline at a glance

100+

proprietary differentiated compounds

multiple families

SBT-272

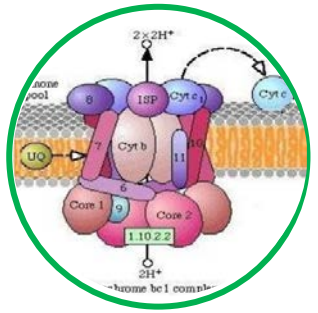
Clinical stage (Phase 1)

↑ mitochondrial uptake (>6X)^

Cmax (~3X), AUC (>25X) in rat brain^

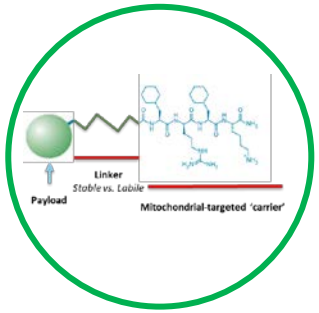
↑ survival in male cohort of ALS SOD-1 model; correlated NfL reduction

↑ neurite length, branching in TDP-43 upper motor neurons



SBT-550

SBT-550 series shows dose-dependent improvements in cell viability in Friedreich's ataxia patient-derived fibroblasts



Delivery

Targeting small molecules to the mitochondria

^ in each case relative to elamipretide; Cmax = maximum concentration; AUC = area under the drug concentration-time curve; NfL = neurofilament light chain

Stealth BT data on file; Keefe et al., *NEALS* 2019; Gautam, et al., *NEALS* 2020; Wu, et.al., J Mol Neurosci., Oct 2018

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Our company at a glance

Leading mitochondrial medicine

Orphan diseases:
Barth (clinical), LHON (clinical), FRDA (clinical), Duchenne (pre-IND), nPMM (clinical), ALS (preclinical)
Age-related diseases:
dry AMD (clinical), glaucoma (preclinical)

Significant unmet need

Visual impairment:
~1m US AMD + ~10k LHON patients
Orphan neurology
Life-limiting cardiomyopathy:
<200 US Barth patients; potential for Duchenne, Friedreich's ataxia

First in class therapies

Fast track:
Barth, LHON, AMD w/GA
Orphan drug:
Barth, LHON
Rare pediatric designation:
Barth
No US approved therapies

Multi-asset platform

Pipeline-in-a-product
100+ pipeline compounds
Mito targeting platform
>600 patents issued + pending

Experienced team

>10 decades drug development experience
Dedicated to improving the lives of patients

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Our team

Reenie McCarthy, Chief Executive Officer

Brian Blakey, PharmD, Chief Business Officer

Jim Carr, PharmD, Chief Clinical Development Officer

Marty Redmon, PhD, Executive VP, Discovery, Development and Technical Operations

Rob Weiskopf, Chief Financial Officer

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