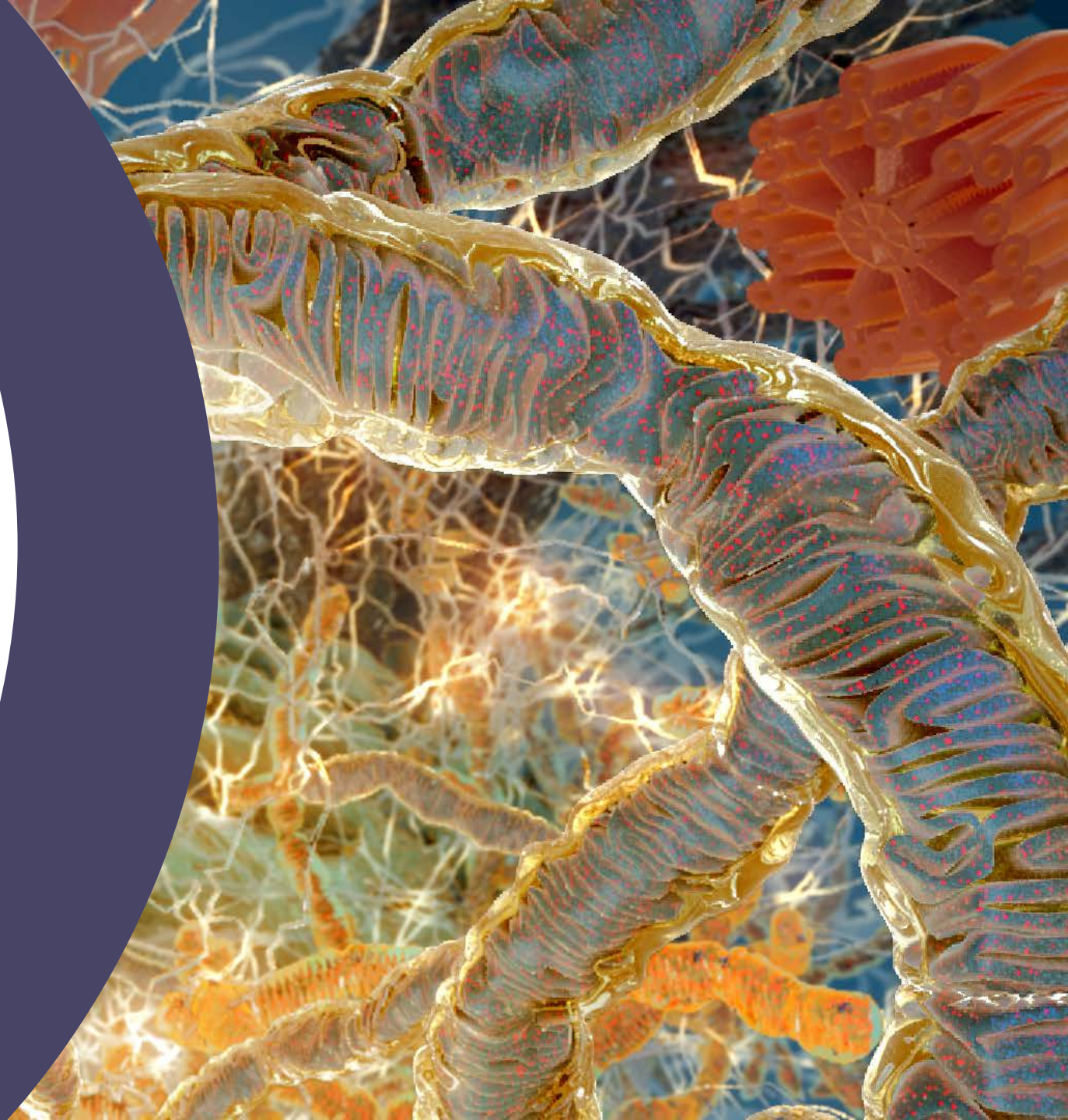
Stealth BIOTHERAPEUTICS

Leading Mitochondrial Medicine

October 2022



Forward-Looking Statements

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.

Key Messages

Late-stage with Strong Platform Potential and Multiple Near-term Inflection Points

- Significant **platform potential** in common age-related and rare diseases
  - Strategy is to **partner common disease programs** and **own US rare disease opportunities**
  - Late-stage programs have been **de-risked by clinical learnings and enrichment strategies**
- Multiple **near-term value inflection points** with late stage elamipretide development programs
- **Deep pipeline** of novel compounds supports expansion and growth

H1 2023

- **Barth** – NDA & partner-ready
- **PMM** - P3 enrollment complete
- **Dry AMD** – partner-ready
- **Friedreich's ataxia** – IND-ready
- **SBT-272** – IND-ready

H2 2023

- **Barth** – pending approval
- **PMM** – P3 read-out imminent
- **Dry AMD** – partnership
- **SBT-272** – partner-ready; P2-ready

2024

- **Barth** – approval, voucher sale & launch
- **PMM** – NDA submission
- **Friedreich's ataxia, DMD** – P2 initiation
- **SBT-272** – P2 initiation

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Allen et al. *Nature Comms Biol* 2020

Unlocking Therapeutic Potential in Mitochondrial Disease

Wholly Owned Clinical Programs Targeting Unmet Need in Ophthalmology, Orphan Diseases and Neurology

Elamipretide Demonstrated Evidence of Clinical Activity

- Dry age-related macular degeneration (AMD) with Geographic Atrophy (GA)
- Primary Mitochondrial Myopathy due to nuclear DNA mutations (nPMM)
- Barth syndrome

Product Candidates Granted Multiple Regulatory Designations

- Fast Track Designation:
  - Elamipretide: dry AMD with GA, nPMM, Barth syndrome
- Orphan Drug Designation:
  - Elamipretide: nPMM, Barth syndrome, Friedreich's ataxia, DMD
  - SBT-272: amyotrophic lateral sclerosis (ALS)
- Rare Pediatric Designation:
  - Elamipretide: Barth syndrome

Anticipated Near-Term Milestones

- Define regulatory path in dry AMD
- Conduct Barth syndrome natural history analyses to inform post-marketing trial design; potential post-marketing trial initiation H1 2023; potential NDA submission H2 2023
- File IND for SBT-272 for ALS (H1 2023)
- Interim data in Friedreich's ataxia P2a trial to inform IND submission H1 2023

Advancing Next-Generation Compounds for CNS Disease

- Phase 1 data for SBT-272 expected YE 2022
- Plan to initiate Phase 2 study of SBT-272 in ALS in 2024
- Progressing SBT-550 series toward pre-IND enabling studies

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Prioritizing Mitochondrial Diseases with Significant Unmet Need

Diseases of Aging

Dry AMD *Leading cause of blindness in older adults which affects ~2 – 6 million US individuals (inclusive of geographic atrophy and drusen stages) with no currently approved therapies. Seeking partnering opportunities.*

Genetic Mito Diseases

nPMM *Rare debilitating muscle disorder affecting ~7,000 US individuals with no approved therapies. In Phase 3.*

Barth syndrome *Rare cardiomyopathy with less than 250 US individuals diagnosed and no approved therapies. FDA discussions ongoing.*

Friedreich's ataxia *Rare neuromuscular, cardiac + vision disorder affecting ~7,000 US individuals with no approved therapies. In Phase 2a.*

DMD cardiomyopathy *Rare neuromuscular + cardiac disorder affecting 12,000-15,000 US individuals with no approved therapies for cardiomyopathy. IND submission planned.*

Neurology

ALS *Rare fatal neurological disorder affecting ~15,000 US individuals with average survival of 3-5 years post-diagnosis. Currently approved treatments provide only modest effects. Phase 1 complete; IND submission planned.*

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Mitochondrial Dysfunction Drives Many Diseases

Impaired Bioenergetics and Oxidative Stress Contribute to Many Age-related and Genetic Diseases

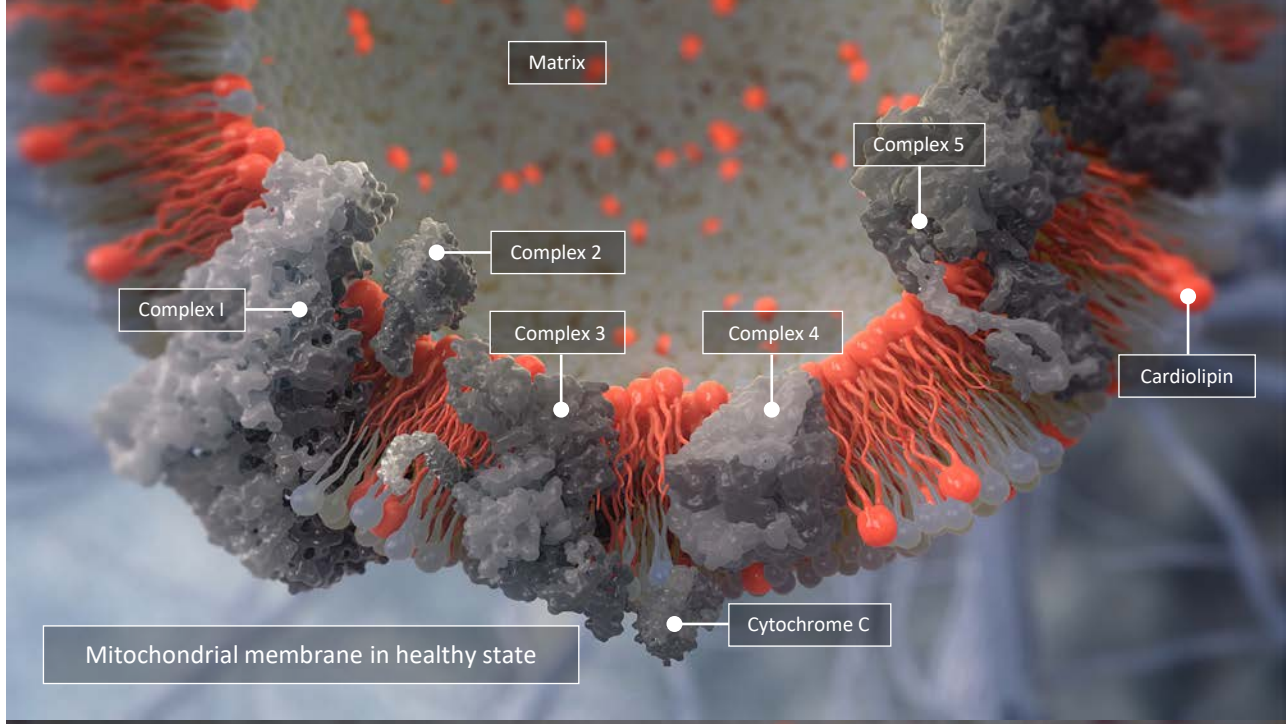
- Mitochondria produce ~90% of the energy utilized by mammalian cells
- Mitochondrial dysfunction is a key driver of rare genetic and common age-related diseases with limited treatment options
- Tissues with greatest energy demand, including the retina, heart, skeletal muscle system and brain, are particularly sensitive to mitochondrial dysfunction

Modified from Suomalainen and Battersby, Nat Rev Mol Cell Biol, 2018

Cardiolipin is Essential for Mitochondrial Function

Altered Cardiolipin Metabolism is Associated with a Range of Mitochondrial Disorders

- Cardiolipin is a mitochondria-specific phospholipid and central regulator of mitochondrial architecture and function
- Cardiolipin-mediated mitochondrial membrane curvature is essential for oxidative phosphorylation, the process by which cellular energy is produced
- In dysfunctional mitochondria, excess reactive oxygen species damage cardiolipin, leading to disrupted membrane curvature, impaired bioenergetics and cell death



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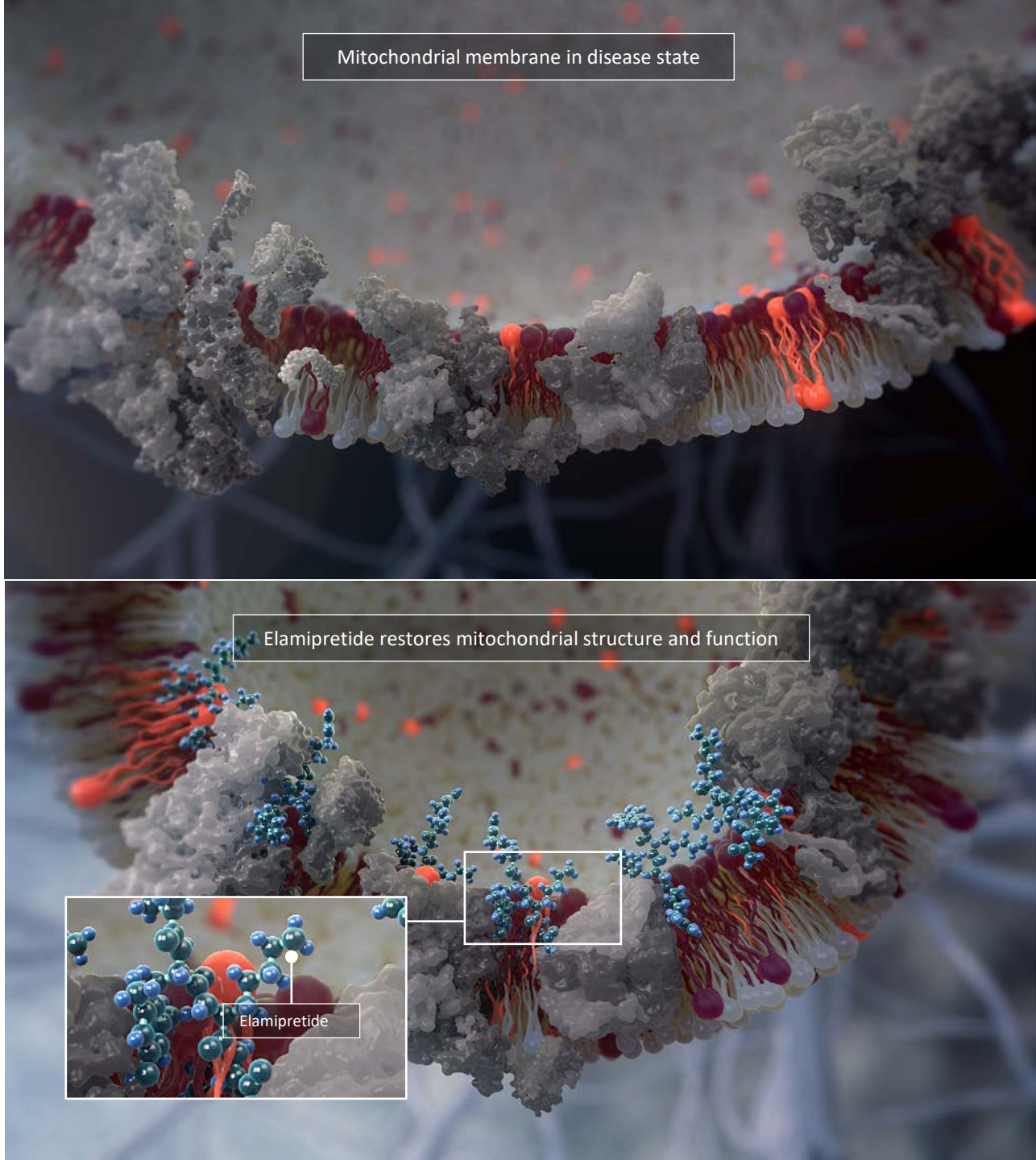
Falabella et al., *Trends Endocrinol Metab,* 2021

Elamipretide Mechanism of Action

Elamipretide Binds to Cardiolipin to Restore Mitochondrial Structure and Function

- ROS-mediated damage of cardiolipin disrupts cristae curvature and organization of respiratory complexes, impairing mitochondrial energy production.
- Cardiolipin damage also leads to impaired mitochondrial protein import and dynamics.
- Elamipretide restores mitochondrial structure and function across preclinical disease models.



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ROS, Reactive oxygen species

Wholly Owned Pipeline Targeting Significant Unmet Needs

INDICATION	CANDIDATE	DISCOVERY	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3
Geographic atrophy (GA) in dry age-related macular degeneration (AMD)	Elamipretide					*Define regulatory path*
Primary mitochondrial myopathy due to nDNA mutations (nPMM)	Elamipretide					*P3 study enrolling*
Friedreich's ataxia	Elamipretide				*P2a study enrolled (investigator sponsored)*	
Duchenne muscular dystrophy (DMD)	Elamipretide				*IND submission planned*	
Barth Syndrome	Elamipretide					*FDA discussions re NDA submission ongoing*
Neurology	SBT-272				*Phase 1 data YE 2022; toxicology studies ongoing; IND submission planned*	
Neurology	SBT-550 series		*Evaluating for Friedreich's ataxia, Leigh's syndrome*			

We aim to progress partnering discussions and pivotal trials in multiple disease indications by early 2023

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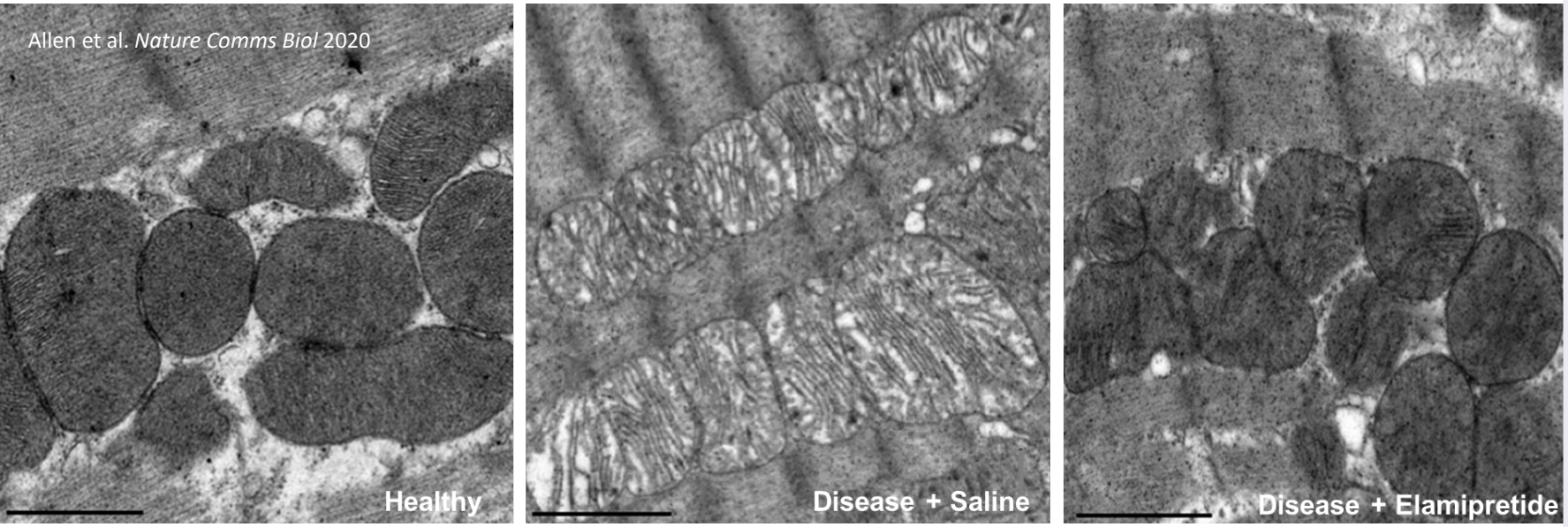
Elamipretide Shows Evidence of Activity in Multiple Preclinical and Clinical Indications

Elamipretide-mediated restoration of mitochondrial structure and function has been shown to improve signs and symptoms of disease in cardiac, ophthalmic and neuromuscular disease models

Improved mitochondrial morphology observed across disease models



Phase 2 study in Geographic Atrophy

Improved vision and demonstrated proof-of-mechanism; first molecule to improve vision in GA

Phase 3 study in Primary Mitochondrial Myopathy

Improved exercise tolerance in patients with PMM caused by nDNA mutations

Phase 3 study in Barth syndrome

Improved cardiac function, exercise tolerance, and muscle strength compared to natural history

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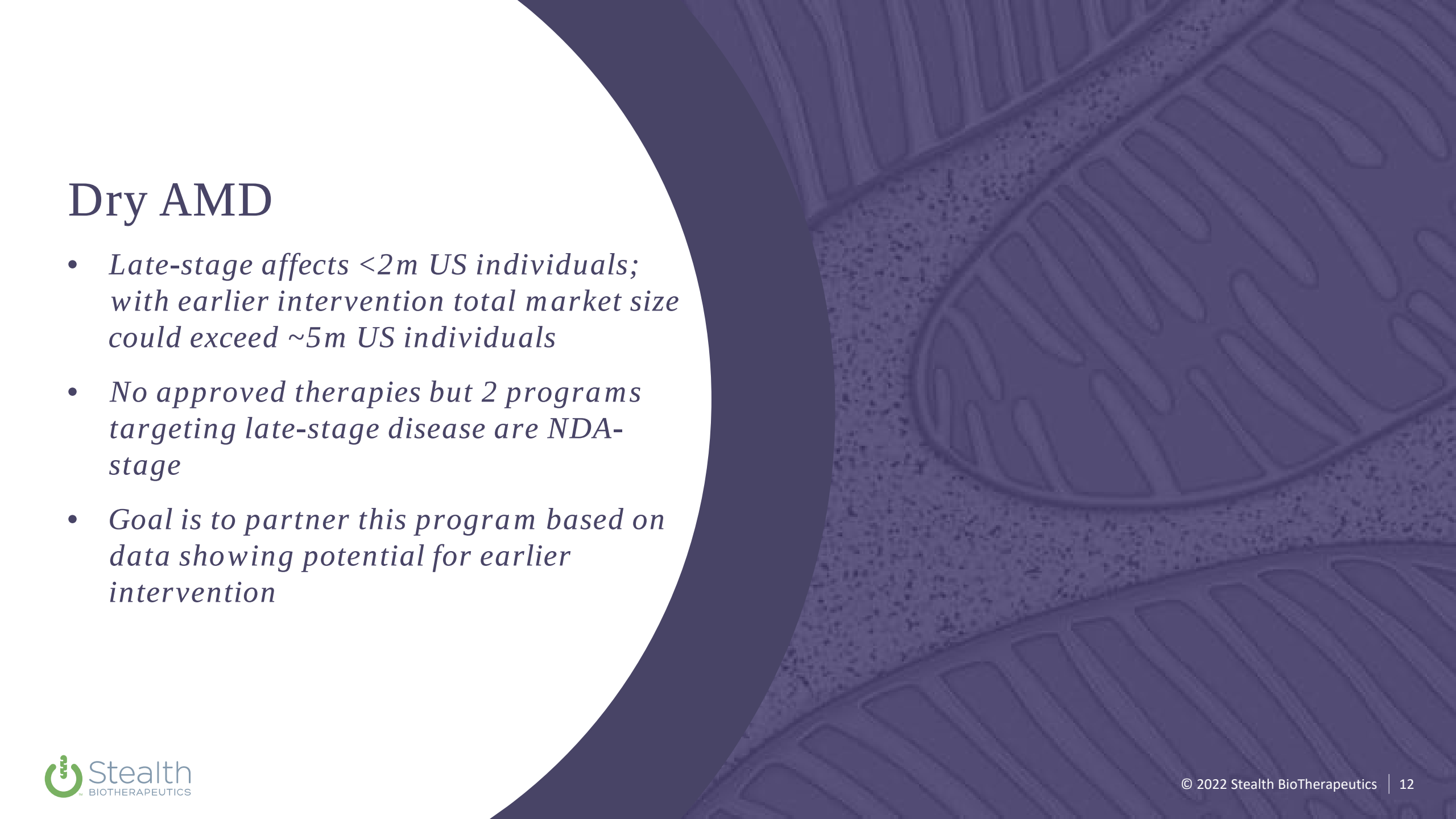
Allen et al. *Nature Comms Biol* 2020

Dry AMD

- *Late-stage affects <2m US individuals; with earlier intervention total market size could exceed ~5m US individuals*
- *No approved therapies but 2 programs targeting late-stage disease are NDA-stage*
- *Goal is to partner this program based on data showing potential for earlier intervention*



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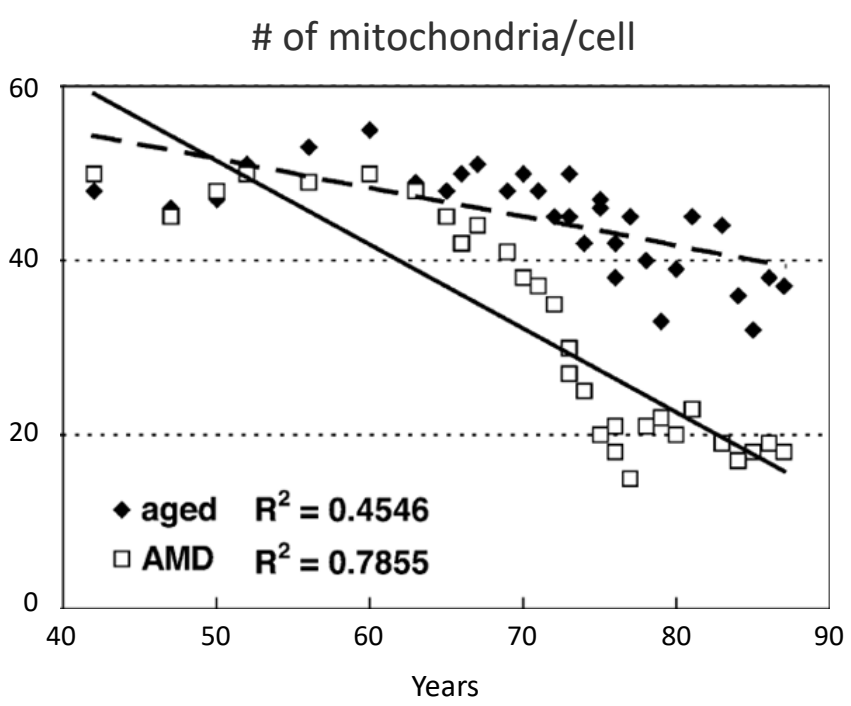
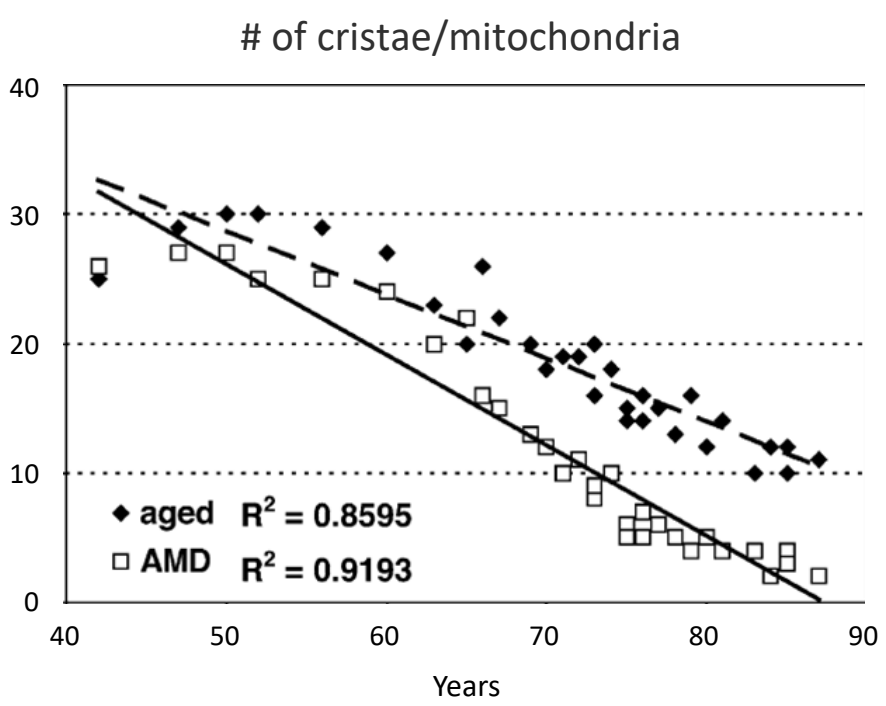
Mitochondrial Dysfunction Precedes Clinical Pathology in GA

Implicated in Activation of the Complement Pathway, Photoreceptor Dysfunction and RPE Cell Death

Degenerative changes in retinal pigment endothelium (RPE) mitochondria in AMD vs. non-diseased aged eyes

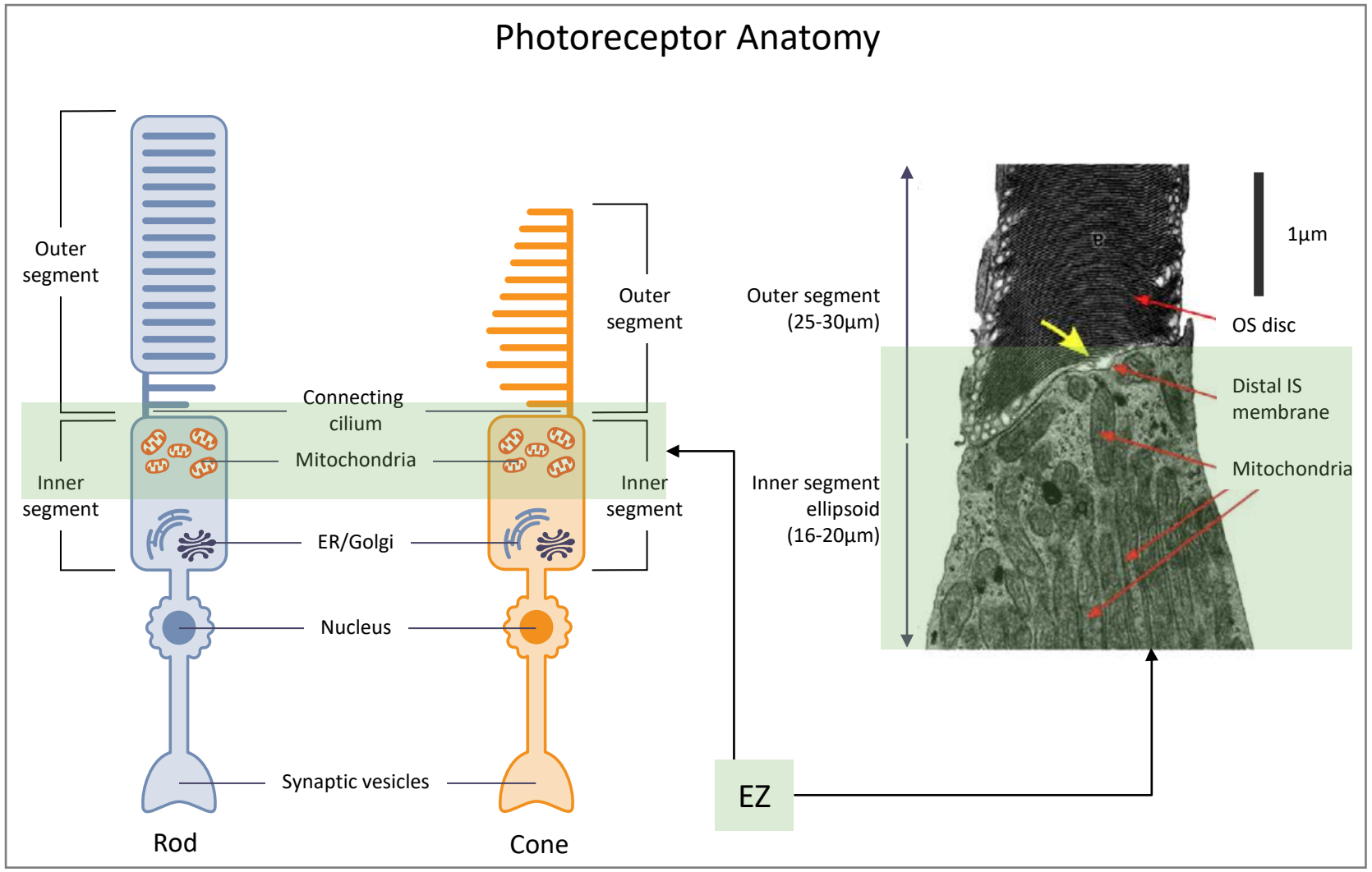




Feher J, Kovacs I, Artico M, et al. *Neurobiol Aging*. 2006;27(7):983-993.

Photoreceptor Loss as an Approvable Endpoint

The Mitochondrial-Rich Ellipsoid Zone (EZ) is a Proxy for Photoreceptor Health



"Preventing photoreceptor loss…would be considered a clinically meaningful endpoint, given the established link between photoreceptor loss and visual function. The threshold of such a therapeutic effect remains to be established." Wiley Chambers, FDA

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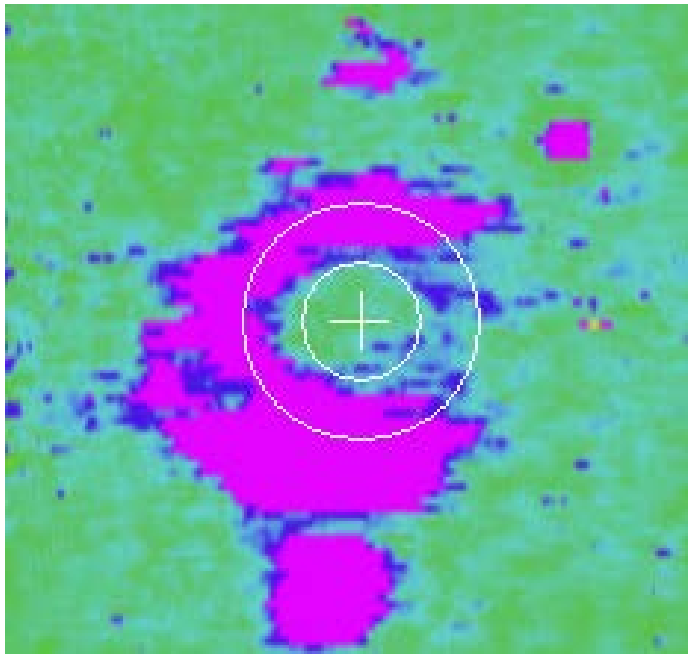
Fu et al., J. Lipid Res. (2021) 62 100035. https://doi.org/10.1194/jlr.TR120000618; Csaki et al., Report From the NEI/FDA Endpoints Workshop on Age-Related Macular Degeneration and Inherited Retinal Diseases, IOVS 2017

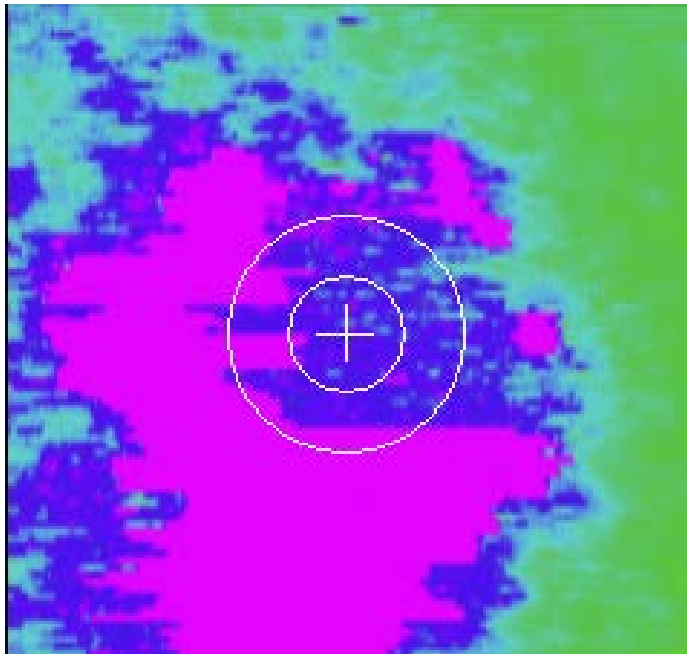
Retinal Mitochondrial Health Predicts Response to Therapy

In Phase 1 ReCLAIM Trial Low Luminance Visual Acuity (LLVA) Changes Correlated with EZ Health

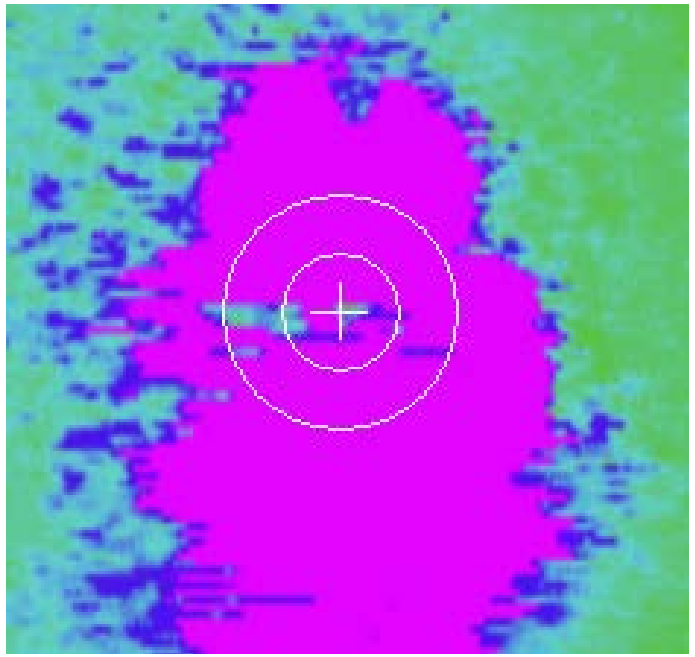
18-letter gain
Patient A: NCGA cohort



4-letter gain
Patient B: NCGA cohort



2-letter gain
Patient C: NCGA cohort

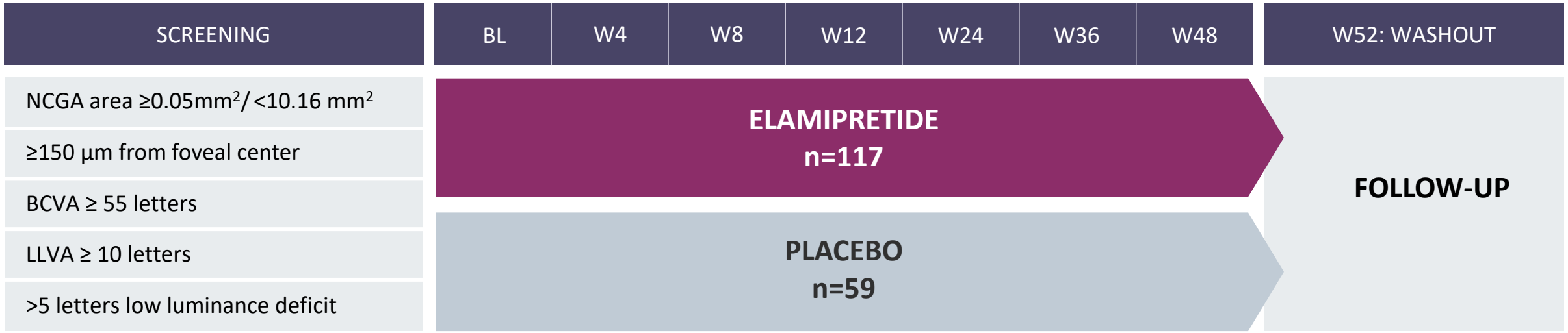


Damaged EZ Healthy EZ

LLVA change inversely correlated with the baseline % macular EZ attenuation (p=0.002)

Correlation analyses were performed post-hoc, statistical analysis showing nominal "p values"

Design of Phase 2 ReCLAIM-2 Trial in GA



Primary Endpoint Family

- Mean change in low luminance best-corrected visual acuity (LLVA)
- Change in geographic atrophy (GA) area by optical coherence tomography (OCT)

Secondary/Exploratory Endpoints

- Categorical change in LLVA
- Ellipsoid zone (EZ) attenuation and associated biomarkers of retinal and mitochondrial health
- Conversion to choroidal neovascularization (wet AMD)

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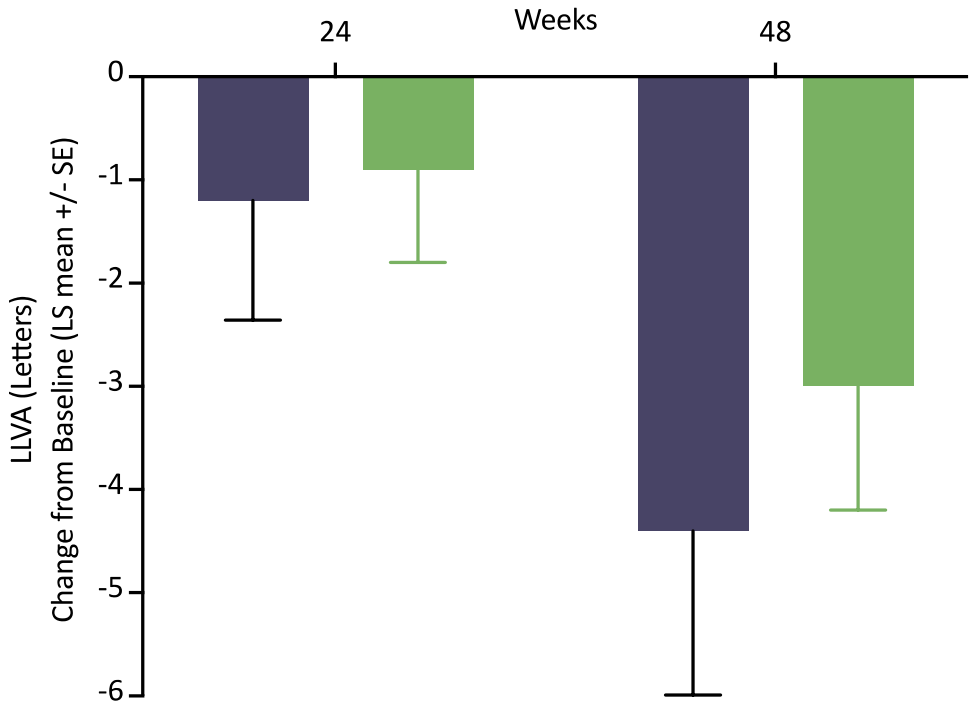
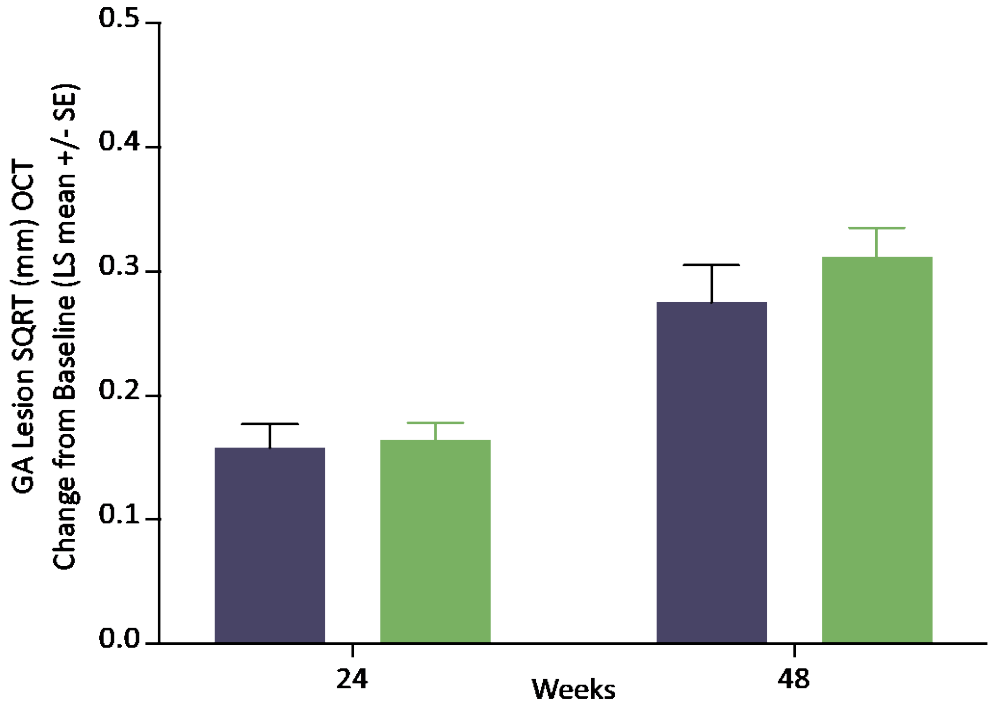
See ClinicalTrials.gov Identifier: NCT03891875 for additional trial details

Phase 2 ReCLAIM-2 Data

Primary Endpoints of Mean Change in LLVA and GA Progression Measured by OCT were Not Significant; LLVA Trend Promising





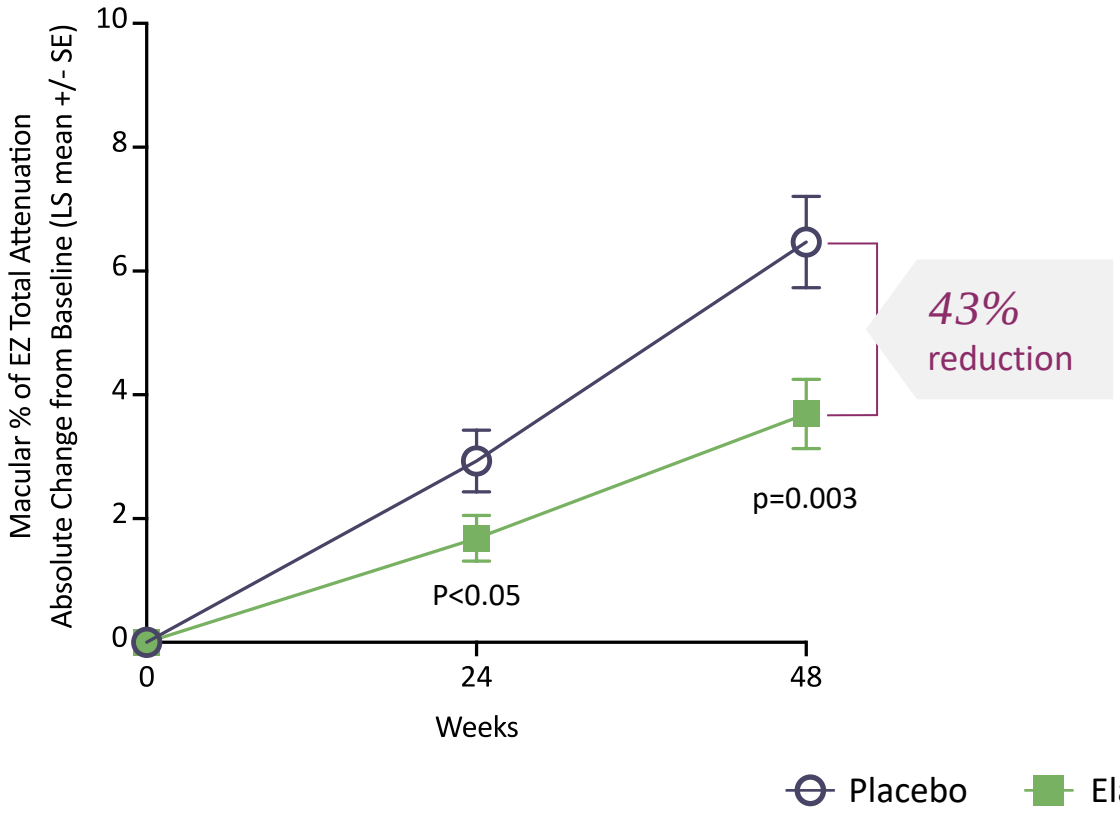
Placebo Elamipretide 40mg

Least Square (LS) means estimated from a mixed-effects model for repeated measures (MMRM). The mITT population was used for the analysis, for LLVA, placebo n=52 and 48 for 24 and 48 weeks, respectively while elamipretide n=93 and 82, respectively. From GA assessment, placebo n=48 and 45, for 24 and 48 weeks, respectively while elamipretide n=89 and 76, respectively.

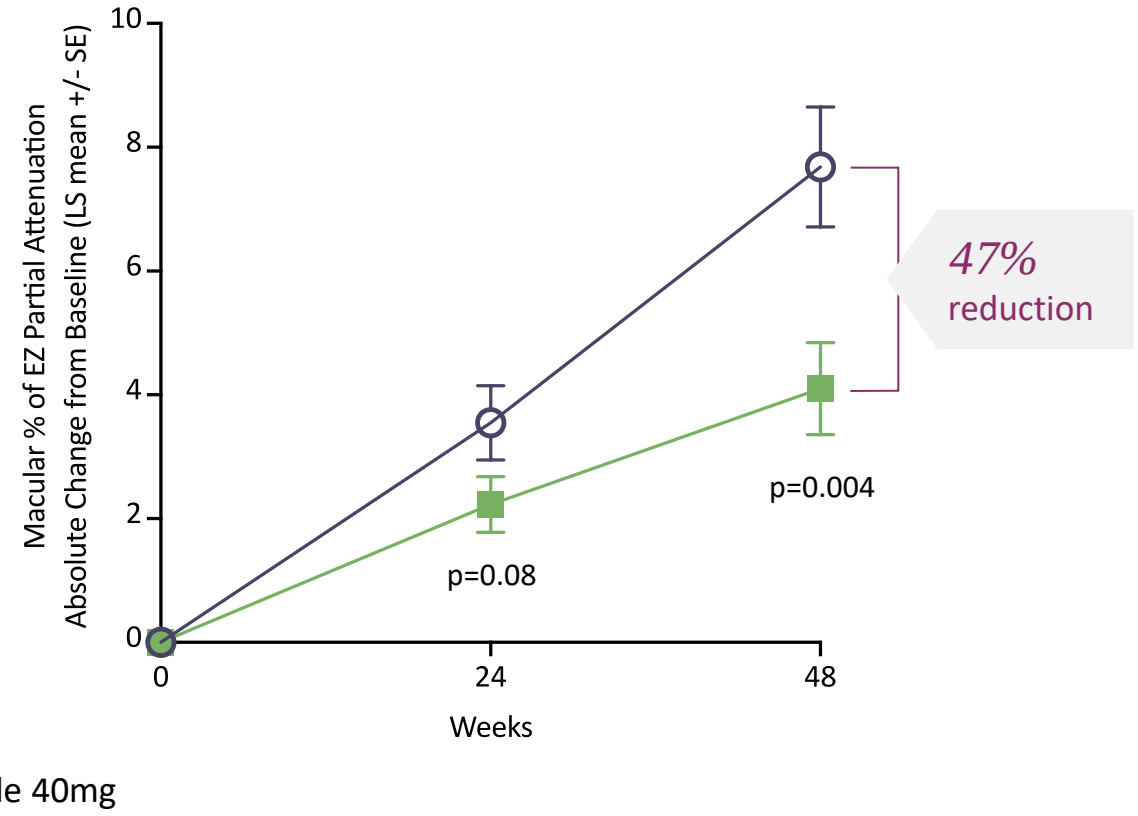
Elamipretide Reduced Attenuation of the Mitochondria-Rich EZ

Prespecified Analysis Provides Proof of Mechanism; Offers Patient Enrichment Strategies for Future Studies

Total EZ Attenuation: thickness of 0 µm on *en face map*



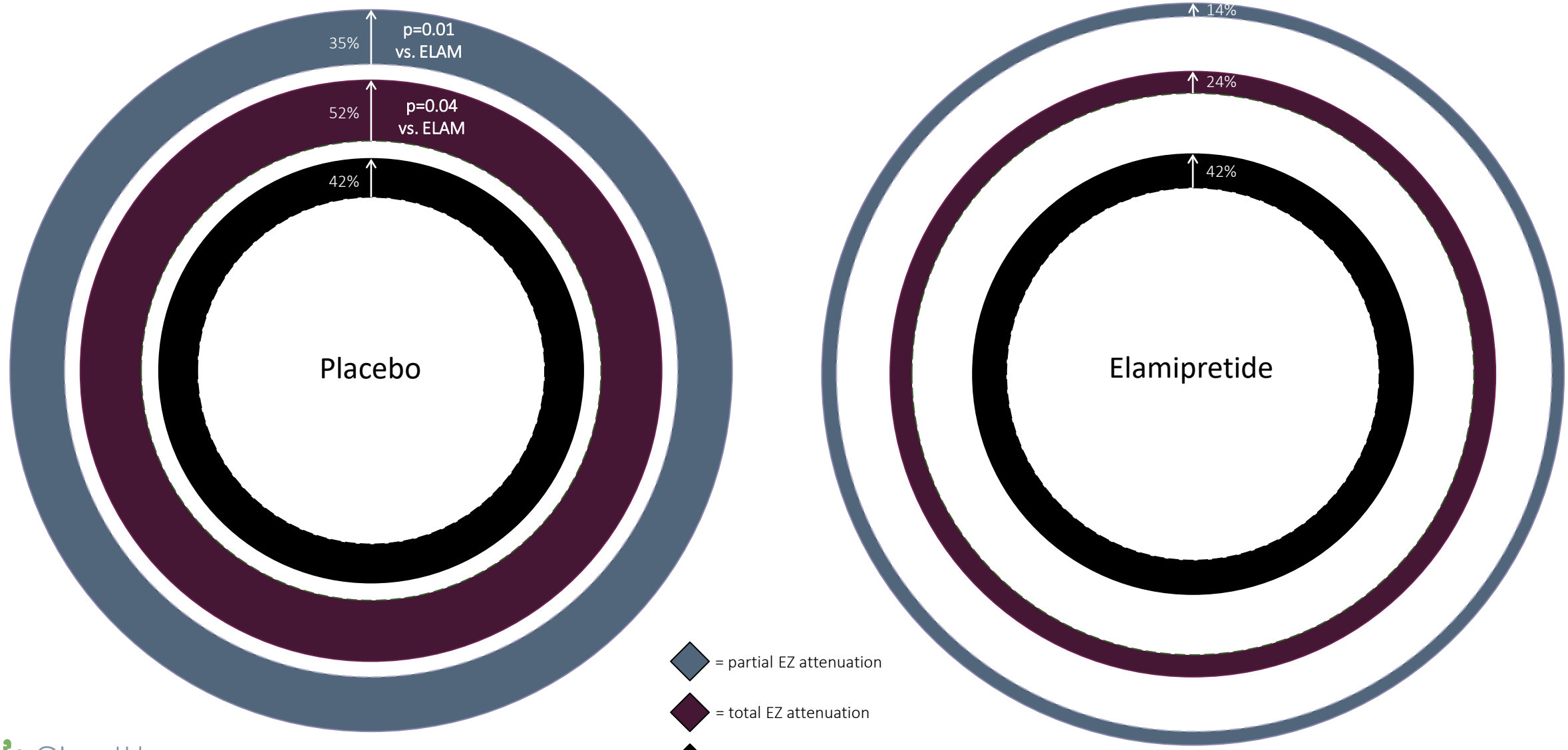
Partial EZ Attenuation: thickness of <20 µm on *en face map*



Placebo Elamipretide 40mg

Least Square (LS) means estimated from a mixed-effects model for repeated measures (MMRM). The mITT population was used for the analysis, for Total Attenuation, placebo n=50 and 42 for 24 and 48 weeks, respectively while elamipretide n=89 and 71, respectively. From Partial Attenuation, placebo n=50 and 42, for 24 and 48 weeks, respectively while elamipretide n=89 and 71, respectively. Statistical analysis showing nominal "p values"

Elamipretide Curtailed Overall Atrophic Progression (EZ + GA)



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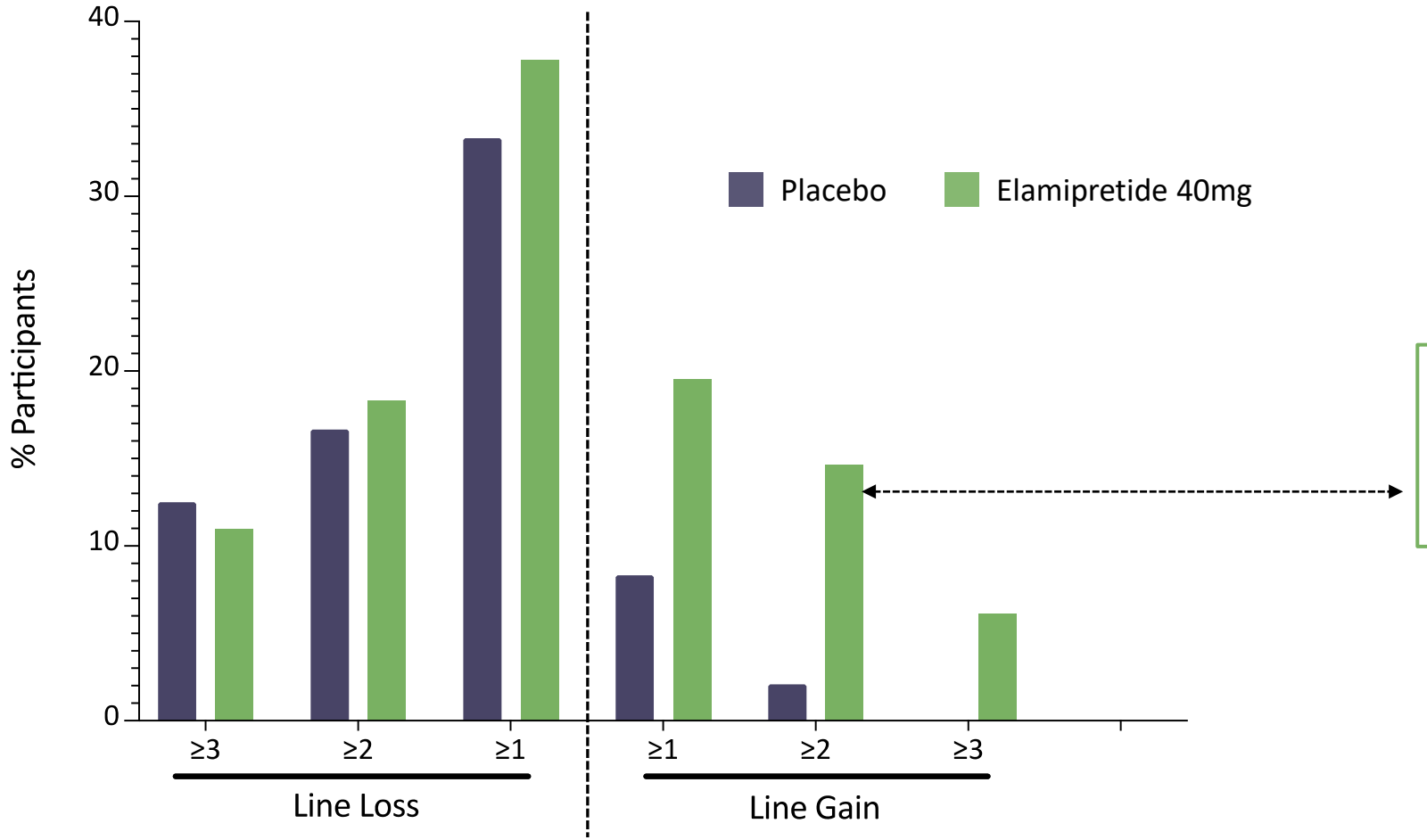
First Investigational Product Shown to Improve Vision in GA

ReCLAIM-2 Pre-specified Analysis Demonstrated Categorical 2+ Line Improvement in LLVA



≥2 Line Gain:
Elamipretide: n=17
Placebo: n=1
P=0.04†

- LLVA change correlated with baseline macular % of total ($p<0.01$) and partial EZ attenuation ($p<0.01$)
- LLVA change correlated with change in macular % total EZ attenuation ($p < 0.01$)

The mITT population was used for the analysis, placebo n=48 and elamipretide n=82.
*Statistical analysis showing nominal "p values", † prespecified endpoint analysis

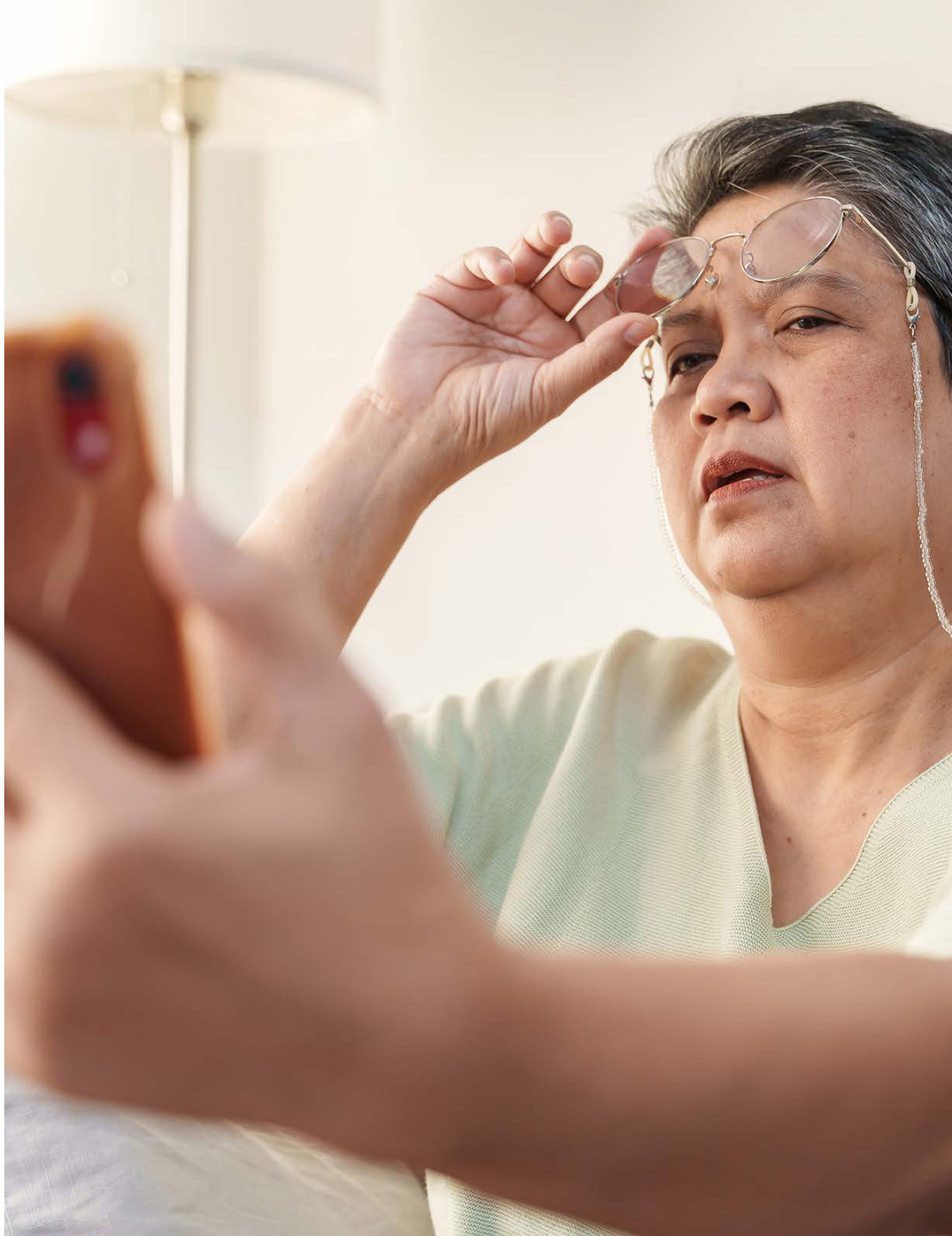
ReCLAIM-2 Data Supports and Informs Further Development

Ellipsoid zone (EZ) attenuation precedes and predicts pathologic changes associated with dry AMD progression

Baseline EZ attenuation correlated with change in LLVA (ReCLAIM, ReCLAIM-2) and GA progression (ReCLAIM-2)

Elamipretide-mediated reduction of progressive EZ attenuation (ReCLAIM-2) correlated with improved visual function (ReCLAIM-2), suggesting the value of EZ attenuation as a surrogate endpoint for dry AMD

Supports development of elamipretide as the first agent shown to improve visual function in GA.



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Barth syndrome

- *Affects <200 US individuals*
- *No approved therapies*
- *Potential gateway to other rare metabolic cardiomyopathies*
- *Rare pediatric designation*

Elamipretide Improves Bioenergetics and Organ Function

Rapid Improvement of Mitochondrial Bioenergetics Followed by Long-Term Improvement in Organ Function

HOURS/DAYS	Improved mitochondrial function *Ex-vivo in explanted human heart tissue*	**Elamipretide Improves Mitochondrial Respiration in the Failing Human Heart** Stauffer, *ESC HF*, 2017, Chatfield, *JACC Basic Translational Sc*, 2019
DAYS	Restoration of healthy gene expression *Cell models*	**Elamipretide remediates respiratory chain and mitochondrial quality control abnormalities caused by cardiolipin deficiency** Anzmann et al; J Biol Chem. 2021
WEEKS	Cardiac/mitochondrial protein turnover *Cell models*	
WEEKS/MONTHS	Improved cardiac substrate metabolism *TAZPOWER P2/3 clinical trial*	**Elamipretide improves plasma medium chain acylcarnitines in Barth syndrome** Oates et al; medRxiv 2020.11.20.20235580
MONTHS/YEAR	Myocardial remodeling *TAZPOWER P2/3 clinical trial*	**Elamipretide improves cardiac parameters in Barth syndrome** Thompson, et al., Genet Med 23, 471–478 (2021)

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Barth Syndrome is a Disease of Cardiolipin Deficiency

Long-term Elamipretide Therapy may Modify Disease Progression

- Barth Syndrome is caused by nuclear gene mutations (TAZ gene) that lead to loss of normal CL, elevations in abnormal MLCL, and mitochondrial respiratory dysfunction
- Elamipretide met the primary and most secondary endpoints in a Phase 3 retrospective natural history control study in Barth Syndrome
- Conducting natural history analyses to inform post-marketing trial design; potential post-marketing trial initiation H1 2023; potential NDA submission H2 2023

Normal cardiolipin (CL)

A “4-legged stool” that creates a wedge-shape facilitating cristae curvature.

Monolysolcardiolipin (MLCL)

A “3-legged stool” that can be embryonic lethal in BTHS, leading to mitochondrial dysfunction and associated disease.

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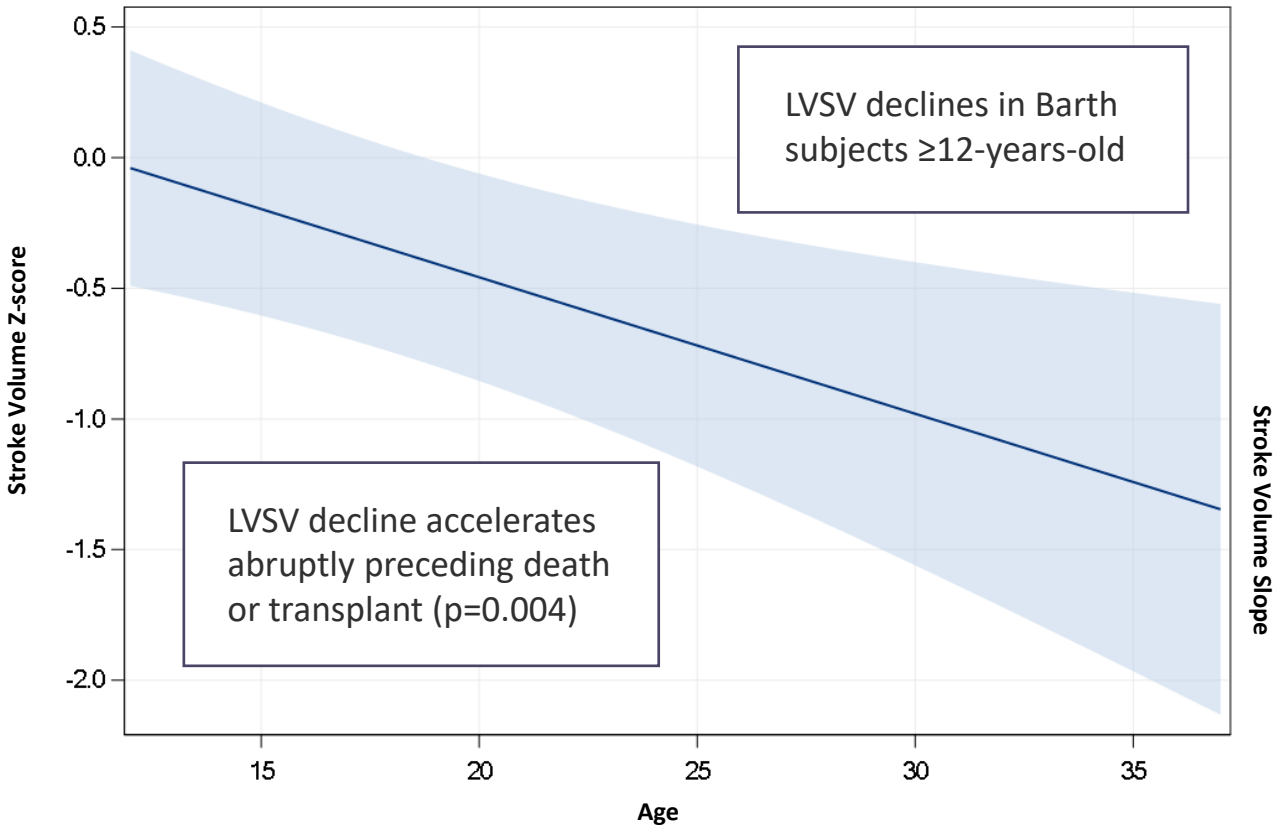
Left Ventricular Stroke Volume (LVSV) Declines in Barth Syndrome

All SPIBA-201 Study Patients were Severely Under-perfused at Baseline; Natural History Predicting Further Declines

Barth Cardiac Natural History



Low BL LVSV for SPIBA-201 Patients Led to Under-Perfusion

Mean SPIBA-201 (n=12) BL cardiac index (CI)	**2.3L/min/m^2 (~3,300 L/day)**
Healthy teenager[2]	~4.13L/min/m2 (6,000-7,500 L/day)
Congestive heart failure[2]	~2.3L/min/m2
Cardiogenic shock[3]	<2.2L/min/m2

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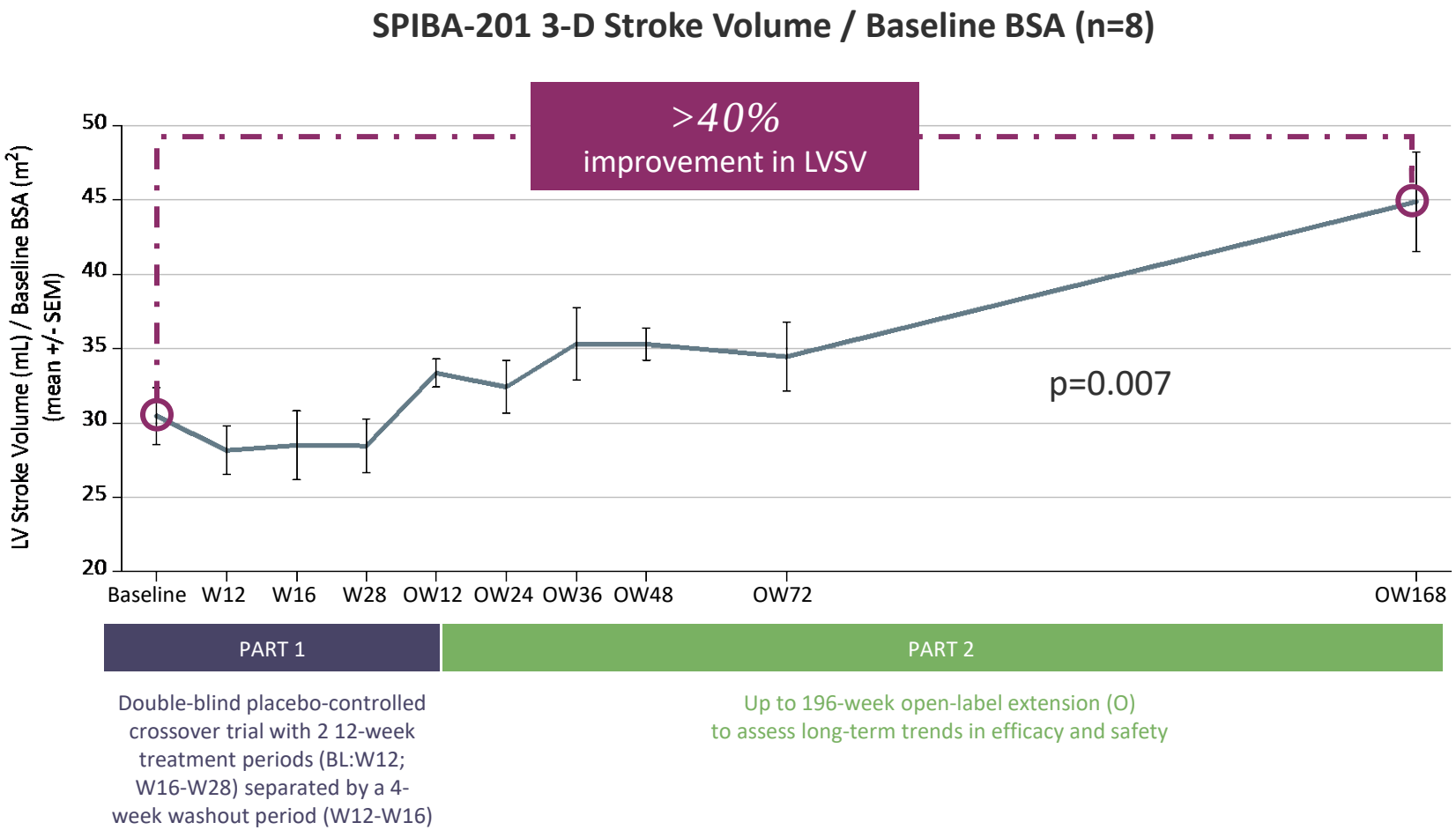
Chowdhury et al., Pediatric Cardiology, 2021

Elamipretide Improved LVSV, Reversing Expected Decline

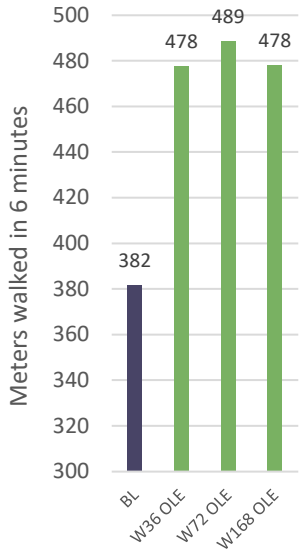
Normalized LV SV for Most Patients with Long-term Therapy Supports Finding of Cardiac Reverse Remodeling



All Functional Improvements Maintained After ~4-years of Therapy

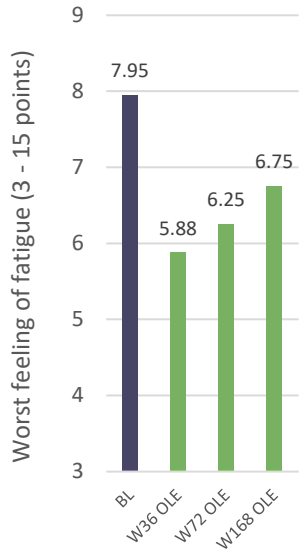
SPIBA-201 Part 2 Demonstrated Increasing Improvements Across Multiple Clinical Endpoints

6MWT (n=8) ↑



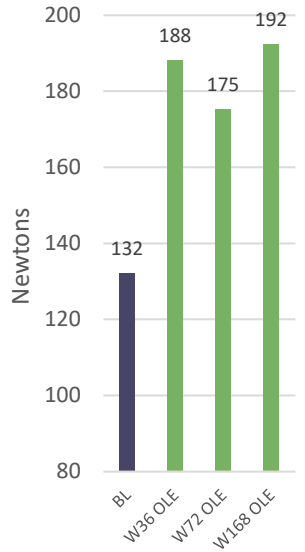
W36 OLE p=0.0241
W72 OLE p=0.0124
W168 OLE p=0.0032

BTHS-SA fatigue (n=8) ↓



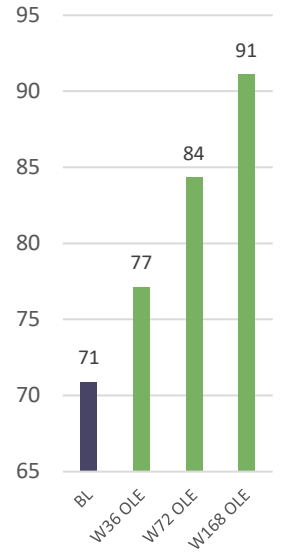
W36 OLE p=0.0312
W72 OLE p=0.0656
W168 OLE p=0.2056

Muscle strength (n=8) ↑



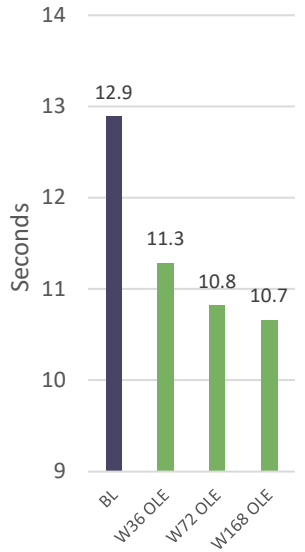
W36 OLE p=0.0009
W72 OLE p=0.0083
W168 OLE p<0.0001

SWAY balance (n=8) ↑



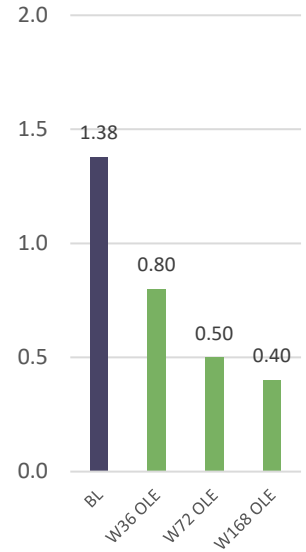
W36 OLE p=0.2038
W72 OLE p=0.0114
W168 OLE p=0.0092

5X SST (n=8) ↓



W36 OLE p=0.2185
W72 OLE p=0.0983
W168 OLE p=0.0900

CGI Symptoms (n=8) ↓



W36 OLE p=0.0950
W72 OLE p=0.0062
W168 OLE p=0.0072

↑ ↓ *denotes direction of positive change*

6 MWT: 6 Minute Walk Test
5X SST: 5 times Sit to Stand Test

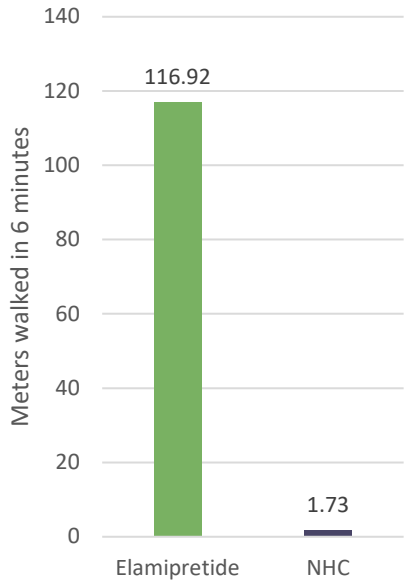
BTHS-SA: Barth Syndrome Fatigue Scale
CGI: Clinician Global Impression

Elamipretide-Mediated Improvements Not Expected in Natural History

SPIBA-001 Phase 3 Trial Comparing Phase 2 OLE Data to Natural History Controls (NHC) Met Primary and Secondary Endpoints

PRIMARY ENDPOINT

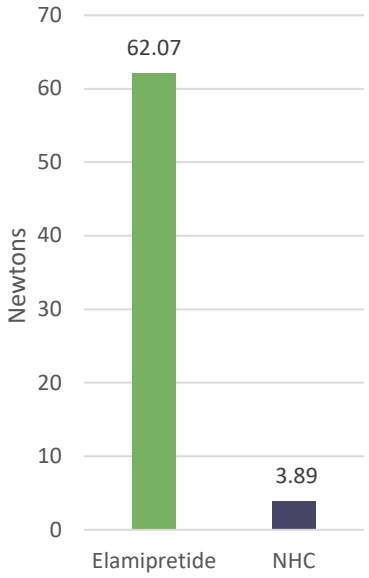
6MWT Δ from baseline



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

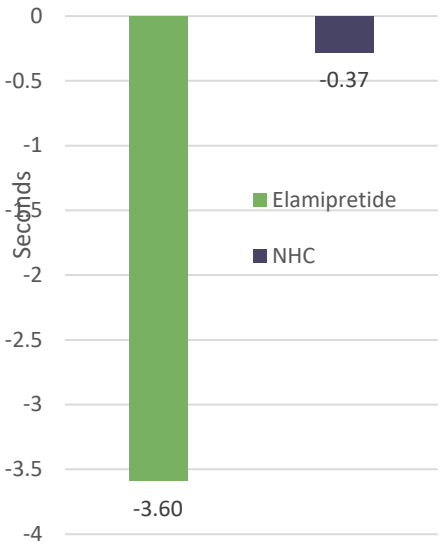
SECONDARY ENDPOINTS

Muscle strength by HHD Δ from baseline



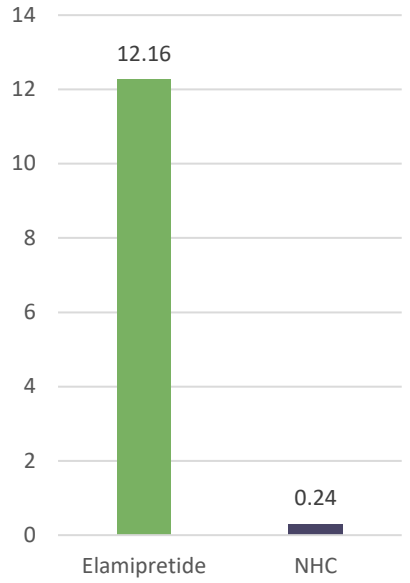
Week 72 OLE: p=0.0002
Week 36 OLE: Elam 41.79, NHC 1.04, p=0.0002
Week 48 OLE: Elam Δ 48.67, NHC Δ 1.97, p=0.0005

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

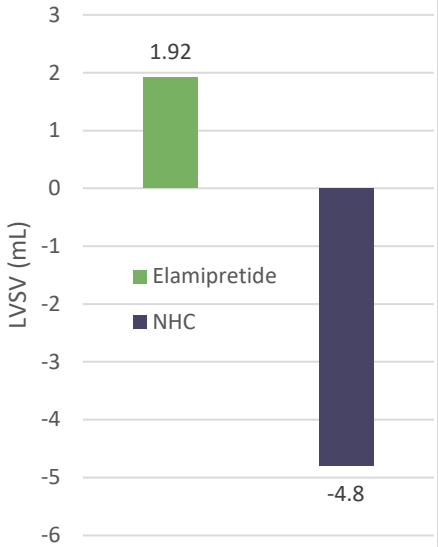
SWAY balance Δ from baseline



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

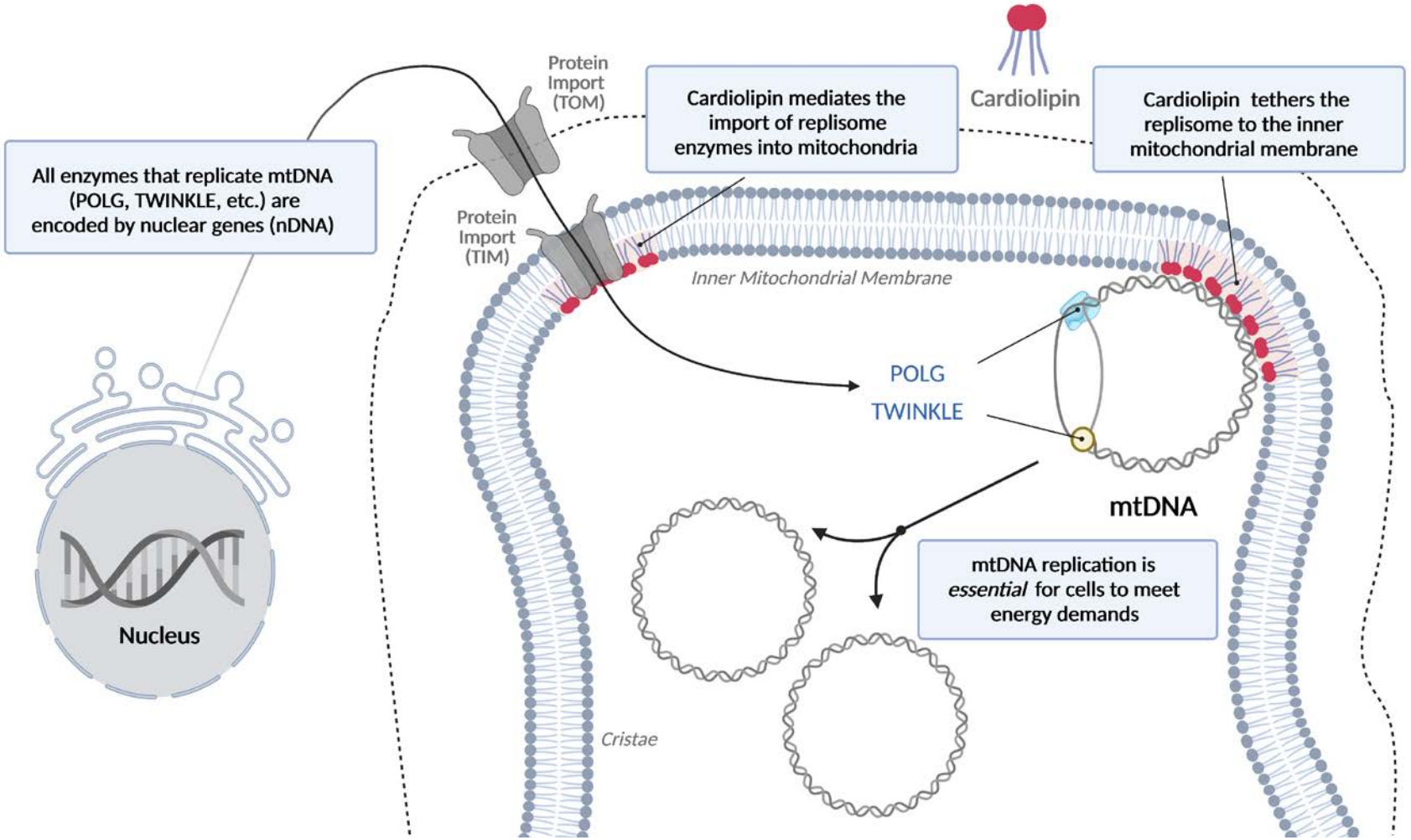
Thompson WR, et al., J Cardiac Failure. October 1, 2020; 26(10);S67. Abstract # 187; Thompson, R., et al, Genet Med. 2020 Oct 2020.

nPMM

- *Affects ~7,000 US individuals*
- *No approved therapies*

Mitochondrial DNA Replication is Critical for Normal Muscle Function

nPMM is Caused by Mutations in nDNA-encoded Proteins Responsible for Replicating mtDNA

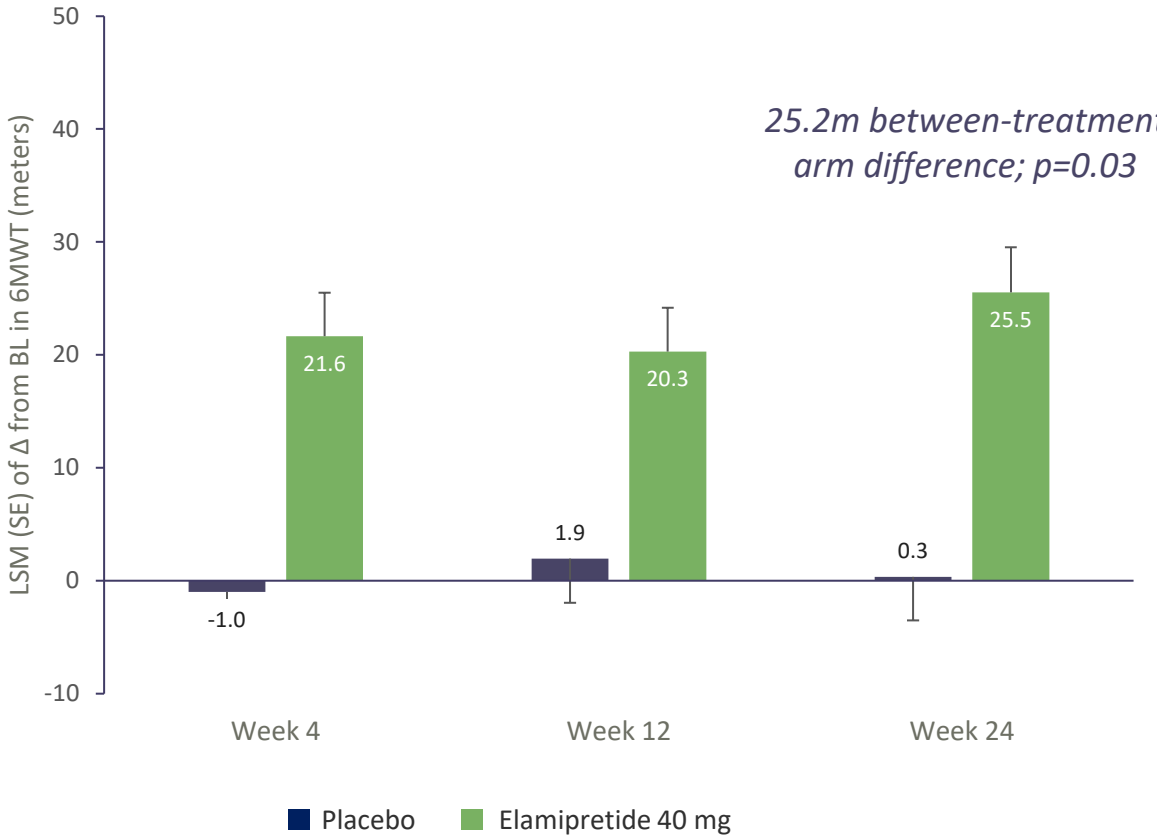


Oliveira et al., Genet. Mol. Biol., 2020; Glancy et al., Nature, 2015; Park et al., Am J Physiol Heart Circ Physiol. 2014; Kukat et al. PNAS 2015

Elamipretide Improved Exercise Capacity in nPMM

MMPOWER-3 Pre-specified Sub-group Analysis can be Supportive of Registration

All nDNA mutations 6MWT *n=59*



Improvements observed in MMPOWER-3 nDNA subgroup

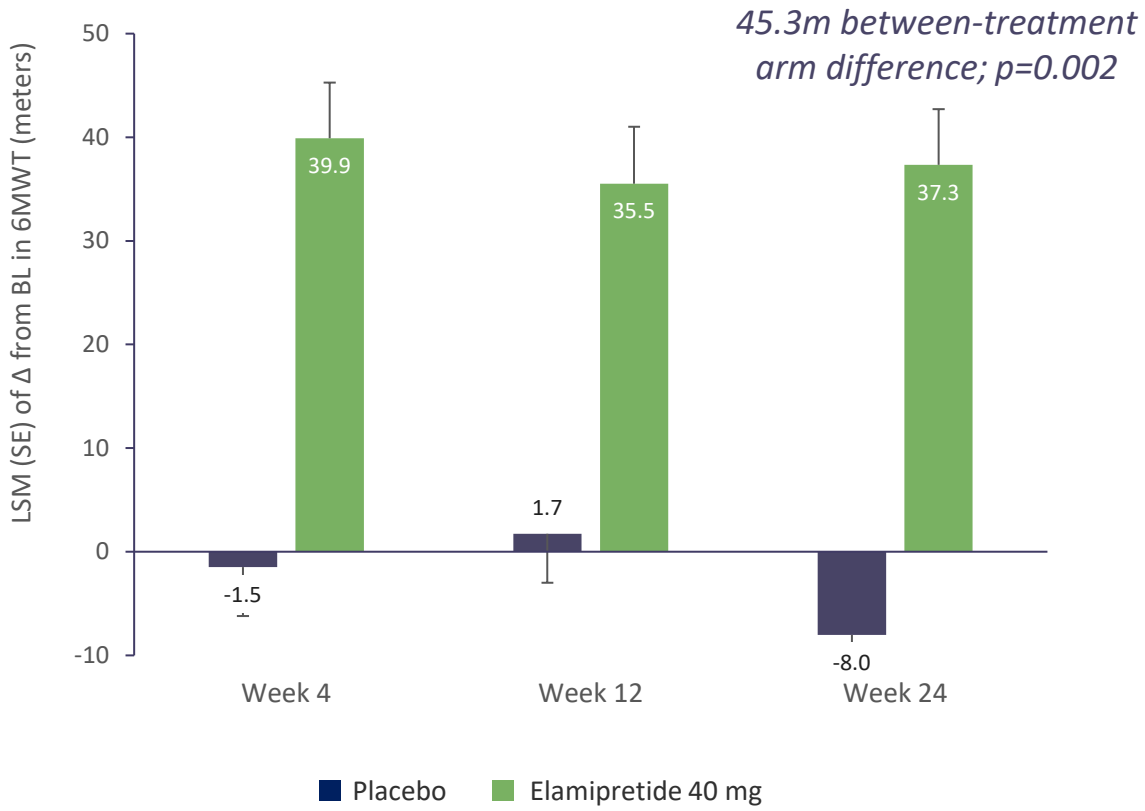
- Phase 3 MMPOWER-3 study enrolled 218 patients with PMM due to mtDNA (~75%) and nDNA (~25%) mutations. Primary endpoints were not met across the full intent-to-treat patient population, which was attributed primarily to heterogeneity of disease presentation across genetic mutations.
- Pre-specified subgroup analysis demonstrated improved 6MWT in nDNA patients (p=0.03; n=59), which can be supportive of registration.
- Exposure-response: Increase in walk distance for subjects with an nDNA mutation was a function of elamipretide drug exposure (p = 0.03)

Stealth BIOTHERAPEUTICS

Phase 3 NuPOWER Trial Enriched for Likely Responders

Post-hoc Analysis of nPMM Patients Meeting NUPOWER Inclusion Criteria Supports Enrichment Strategy

Replisome-related nDNA mutations + PEO 6MWT *n=32*



Enriching Strategy to Predict More Robust Response

- nPMM can affect multiple organ systems. Ensuring a primarily myopathic disease presentation is important to reduce heterogeneity in clinical trial design.
- Patients with a primarily myopathic disease presentation typically experience ocular muscle involvement, characterized by progressive external ophthalmoplegia (PEO). 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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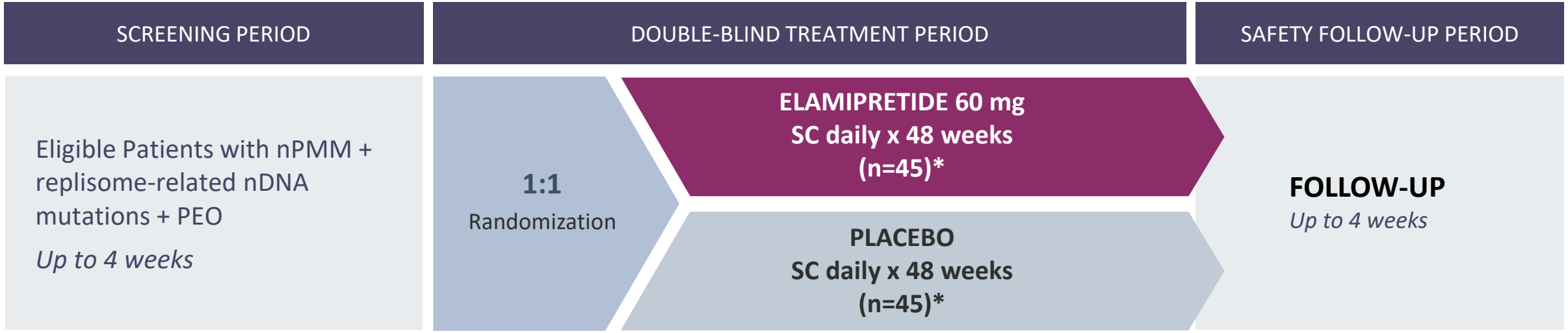
Phase 3 NuPOWER Trial in nPMM Currently Recruiting



Primary Endpoint

- 6 Minute Walk Test (6MWT)

Secondary Endpoints

- 5 times sit-to-stand Test (5XSST)
- 3 times up-and-go Test (3TUG)
- Patient Reported Outcomes

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

Friedreich's ataxia

- *Affects <7,000 US individuals*
- *No approved therapies*

Friedreich's Ataxia is Caused by nDNA Mutations Affecting Mitochondrial Function

Fully-enrolled Investigator Sponsored Phase 2a Trial to Inform Potential 2023 IND Submission

- Friedreich's ataxia is caused by nuclear gene mutations (FXN gene) that lead to mitochondrial dysfunction
- Patients experience progressive ataxia, cardiomyopathy, and visual dysfunction
- Elamipretide improves frataxin expression and mitochondrial function in patient-derived lymphoblasts and improves motor and cardiac function, frataxin expression and mitochondrial function in frataxin-deficient mice
- Interim data from fully-enrolled Phase 2a investigator sponsored study assessing the effect of elamipretide on visual and cardiac function is expected H1 2023 and will inform IND submission.

Stealth BIOTHERAPEUTICS

Zhao, et al., Scientific Reports, 2017; Liu et al., Hum. Mol. Gen. 2021.

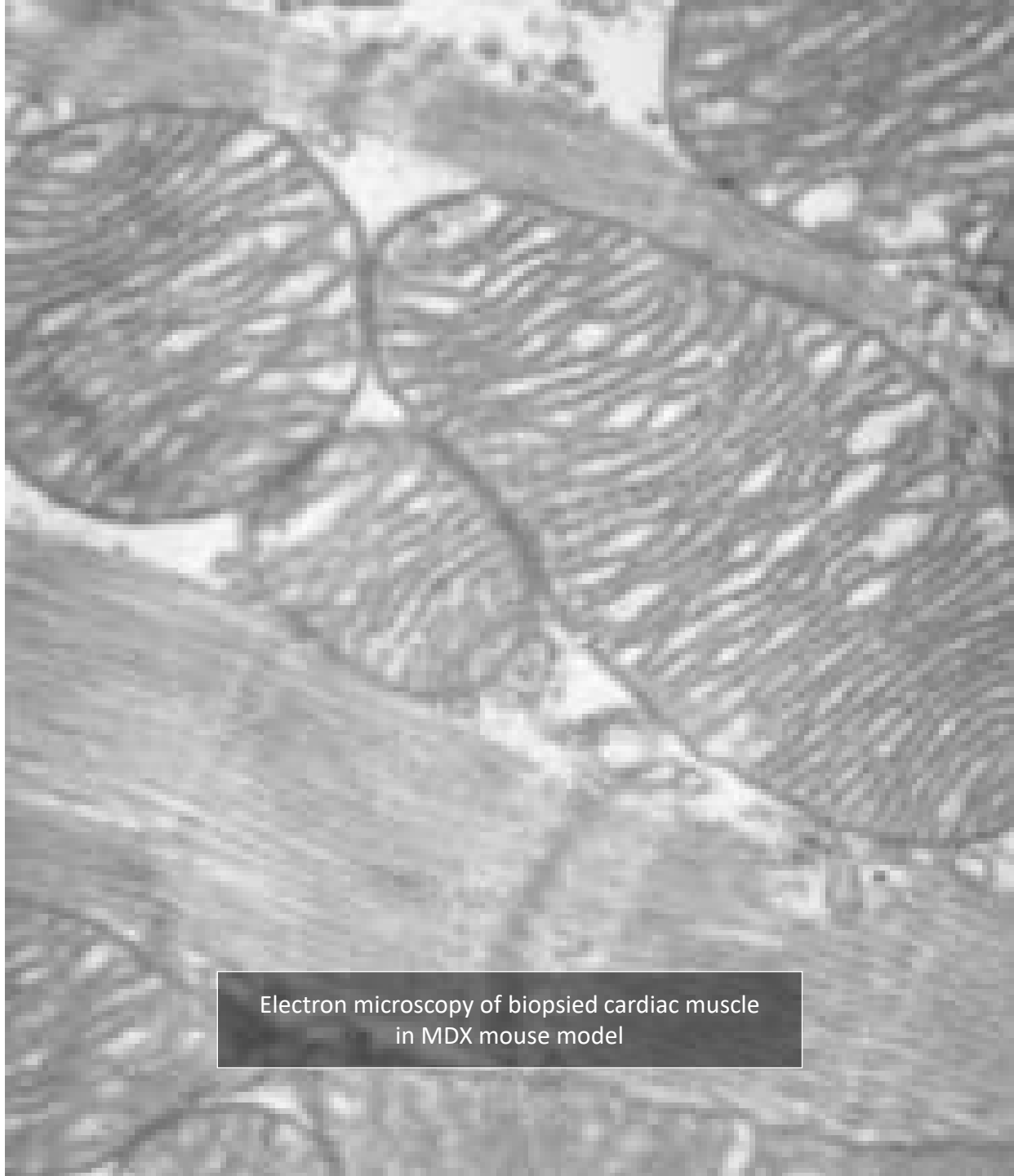
DMD Cardiomyopathy

- *Affects 12,000-15,000 US individuals*
- *No approved therapies*

DMD is a Mitochondrial Disease

Elamipretide may Address Unmet Need in DMD Cardiomyopathy

- Mitochondrial dysfunction is an early part of the pathological cascade in DMD
- Impaired mitochondrial bioenergetics are observed *before* declines in muscle and cardiac function across species
- We are evaluating the potential of elamipretide to address DMD cardiomyopathy, the leading cause of death in DMD
  - Average age of death for patients with DMD cardiomyopathy is 19.6 years old
- There are no approved therapies for DMD cardiomyopathy



Electron microscopy of biopsied cardiac muscle in MDX mouse model

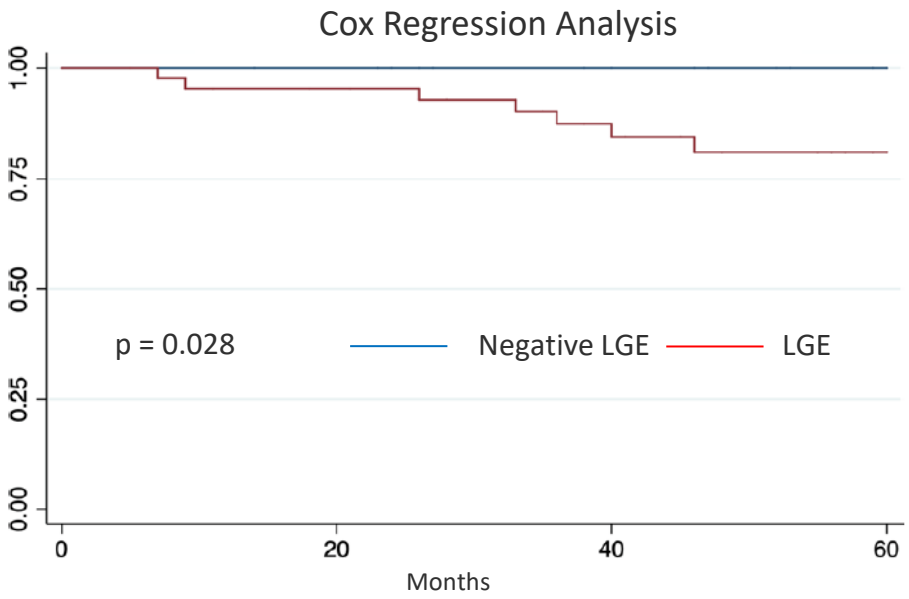
Meyers, Townsend, Int J Mol Sci. 2019; Nigro, Acta Myol. 2012; Payne, R.M., Prog. Pediatr. Cardiol., 2011; Giugliano, GR et al., Tex Heart Inst J, 2007; Machiraju et al., Front Cardiovasc Med 2019.

Stealth BIOTHERAPEUTICS

Potential of Elamipretide to Treat DMD Cardiomyopathy

FDA is Aligned on Proposed Fibrosis Surrogate Endpoint

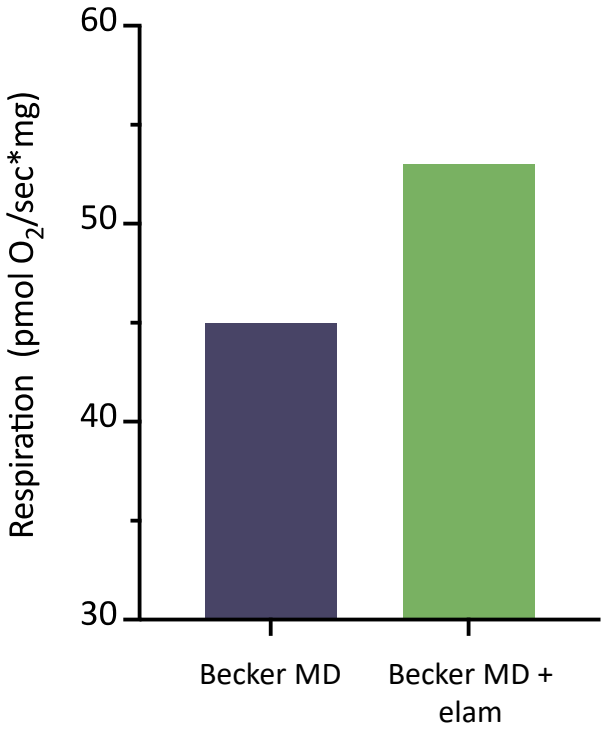
Fibrosis is associated with poor outcomes in DMD



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

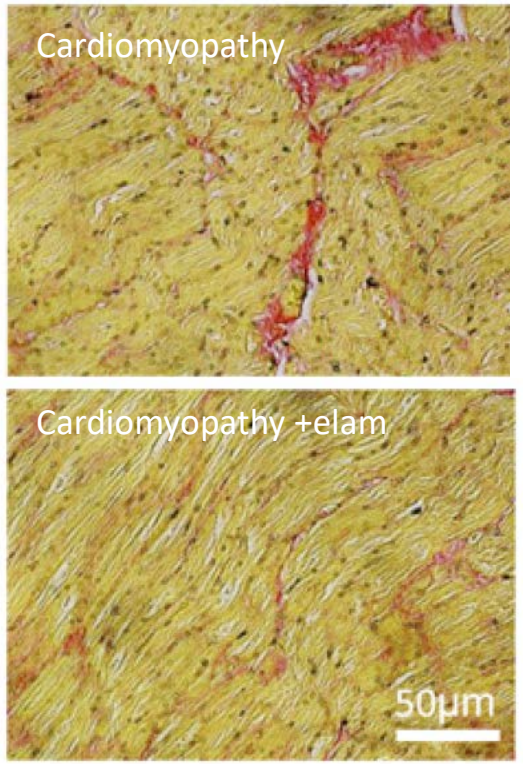
Raucci et al., J Cardiovasc Magn Reson, 2021.

Elam improves mitochondrial respiration in a dystrophic human heart



Stauffer, unpublished, 2020; Hughes, 2019.

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



Red = fibrotic tissue

Eirin et al., JAHA 2016

SBT-272 for Neurological Disease

- *Amyotrophic lateral sclerosis (ALS) (lead indication) affects ~16,000 US individuals*
- *Orphan drug designation granted*

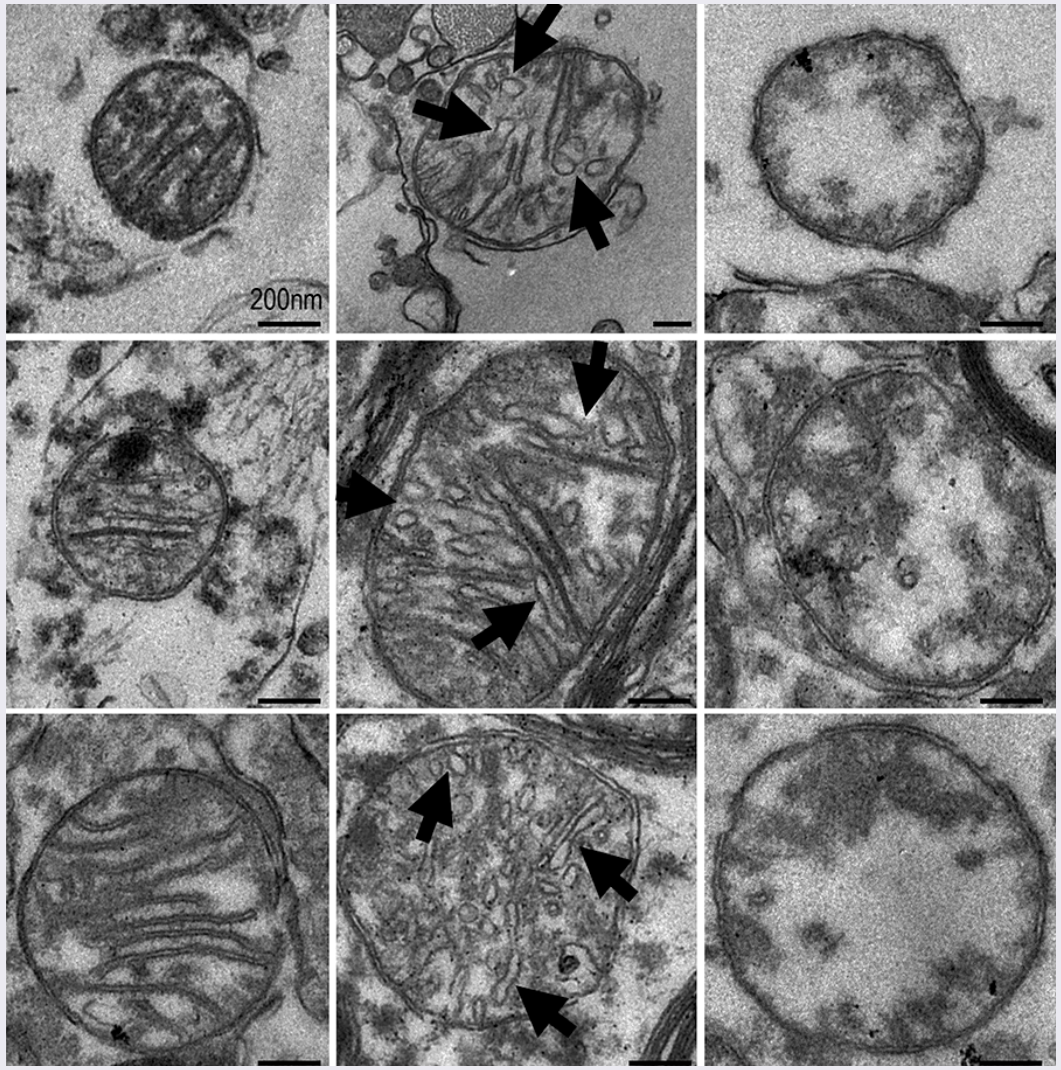
Mitochondrial Dysfunction Characterizes Neurodegenerative Diseases

Implicated in ALS, Frontotemporal Lobar Dementia (FTD), Parkinson's, Alzheimer's, Huntington's, Among Others

- Mitochondrial dysfunction in neurodegenerative diseases can affect mitochondrial respiration (ATP production), electron transport chain complexes, calcium handling, mitochondrial dynamics (fission and fusion), mitochondrial biogenesis, protein synthesis and apoptotic signaling.
- In ALS, mitochondrial dysfunction may cause motor neuron death by predisposing them to calcium-mediated excitotoxicity, by increasing ROS generation and by initiating the intrinsic apoptotic pathway.

Wang et al., PLOS Genetics, 2019; Manfredi et al., Mitochondrion, 2005; Smith et al., Neuroscience Letters, 2019; Golpich et al., CNS Neuroscience & Ther., 2016.

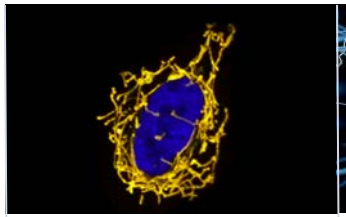
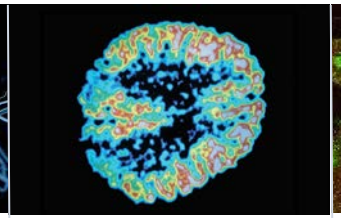
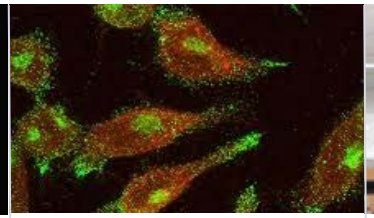
Mitochondria in Brain Tissue of Patients with TDP-43 Pathology (implicated in ALS, FTD)



Stealth BIOTHERAPEUTICS

SBT-272 is Neuroprotective Across Neurological Disease Models

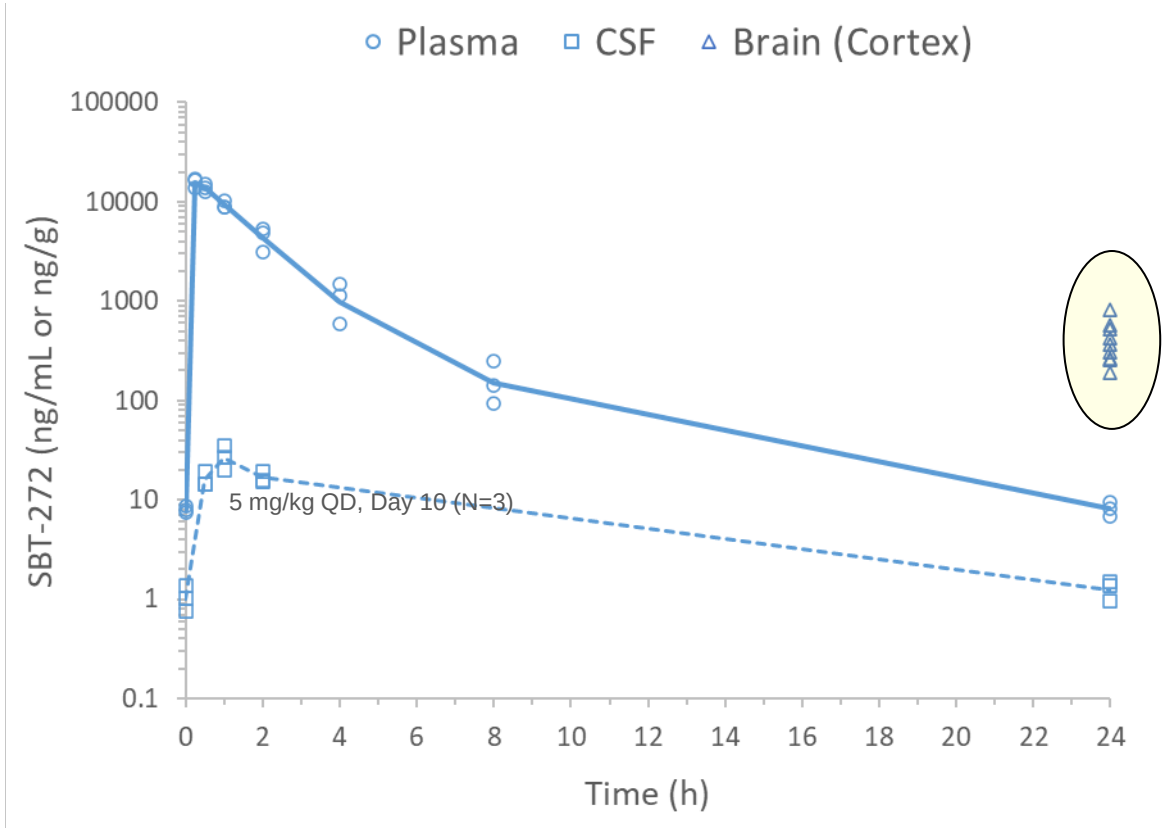
Consistency of Signal may Suggest Platform-in-product Potential. ALS and FTD are Indications of Interest.

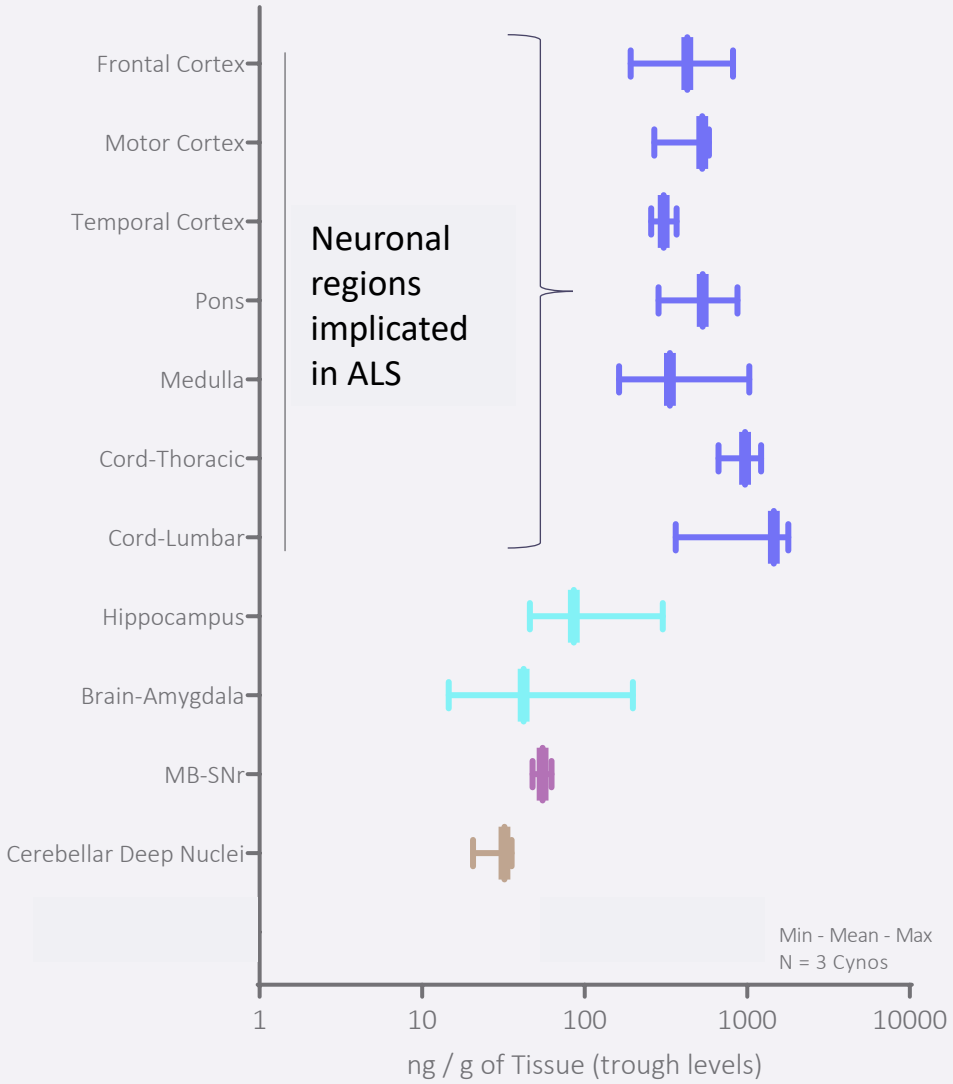
	 Mitoprotection	 Neuroprotection	 Brain metabolism	 ↓ protein aggregates	 ↓ motor deficit	 ↓ inflammation
Amyotrophic lateral sclerosis	✓ TDP-43	✓ TDP-43			✓ SOD-1	
Frontotemporal dementia	✓	✓		✓		
Alpha-synucleinopathy	✓	✓		✓		✓
Huntington's disease*	✓		✓		✓	
Cerebral ischemia reperfusion	✓					

Stealth BIOTHERAPEUTICS

Therapeutic Concentrations in Key Neuronal Regions Implicated in ALS

Monkey PK and Brain biodistribution after 10 days at NOAEL (5 mg/kg)



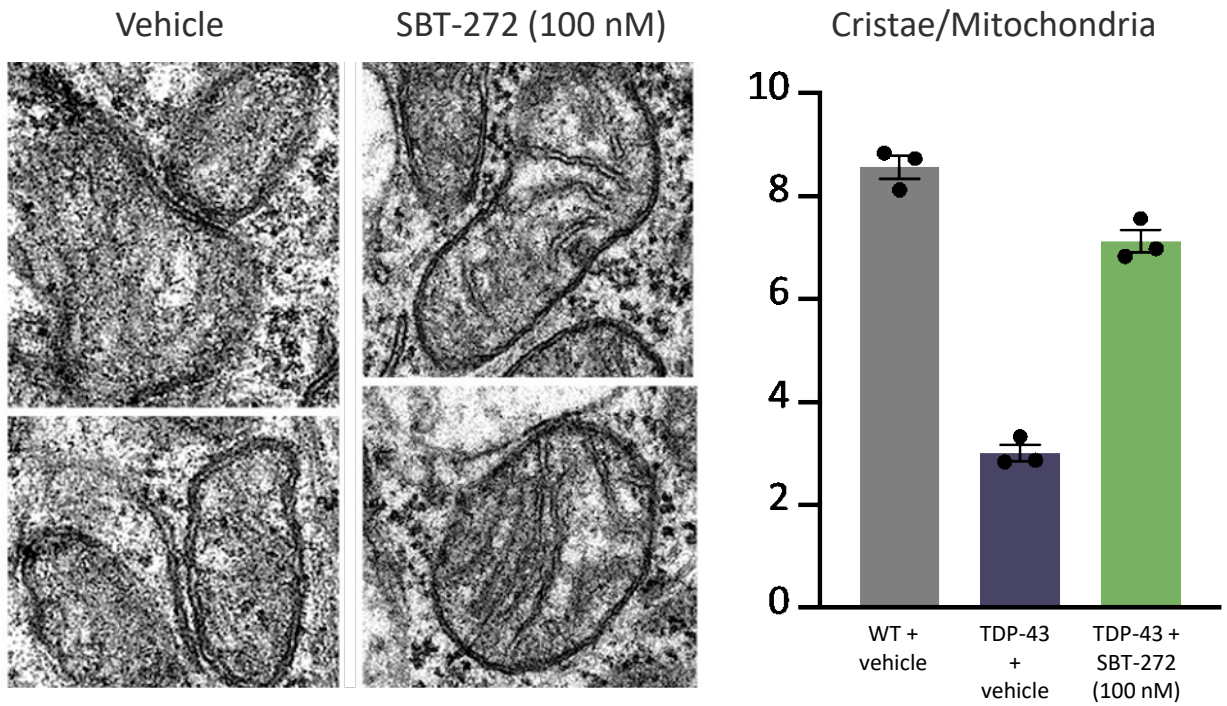


Stealth BIOTHERAPEUTICS

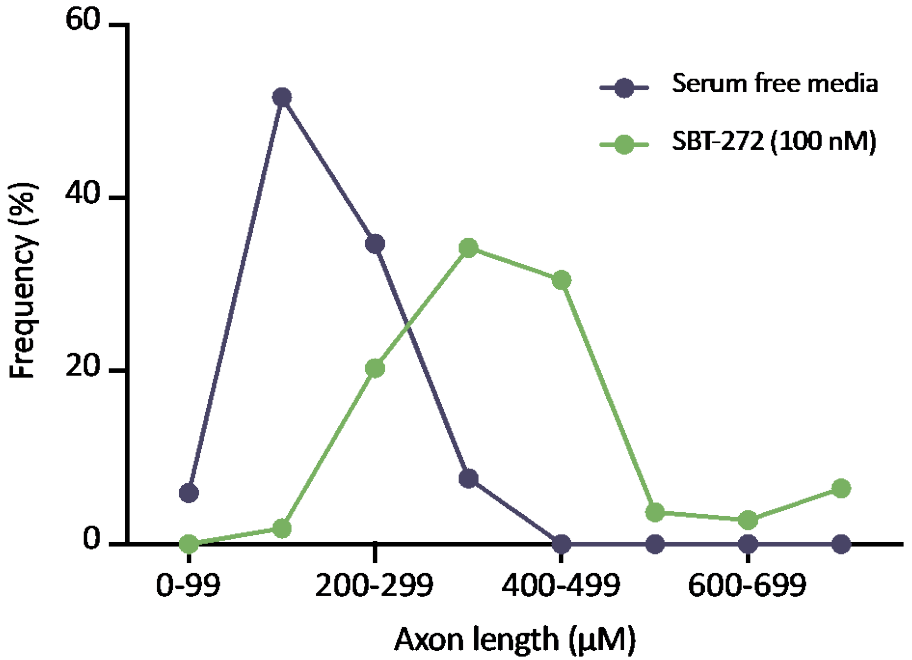
SBT-272 Improves Mitochondrial and Neuronal Health in ALS Model

TDP-43 Pathology is Also Implicated in Frontotemporal Dementia (FTD)

SBT-272 Restores Mitochondrial Cristae Architecture in TDP-43 Cultured Neurons



SBT-272 Increases Axon Length in TDP-43 Cultured Neurons



SBT-272 Improves Mitochondrial and Neuronal Health in ALS Model

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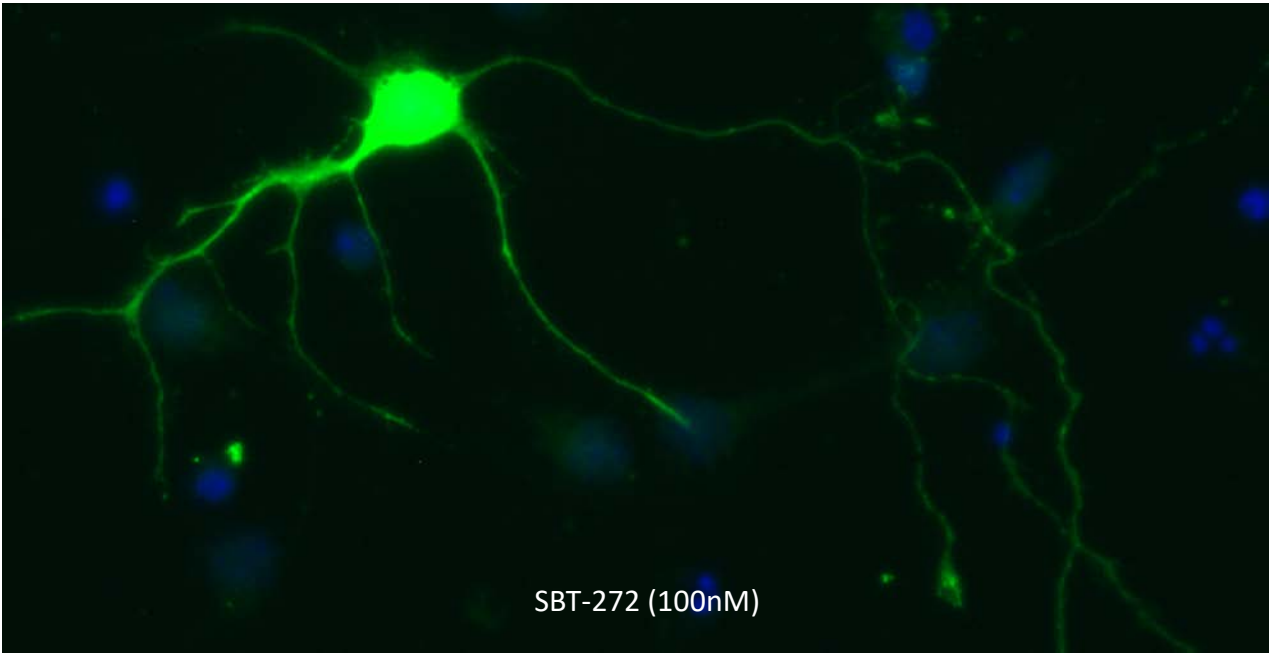
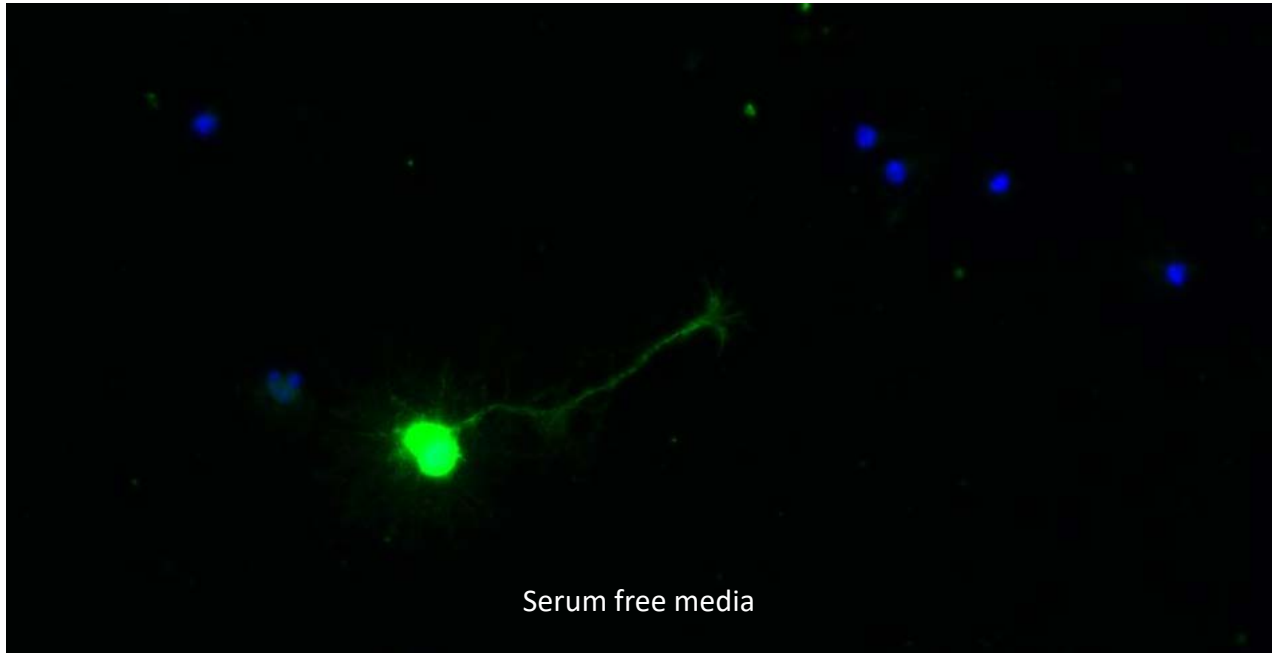
SBT-272 Increases Axon Length in TDP-43 Cultured Neurons

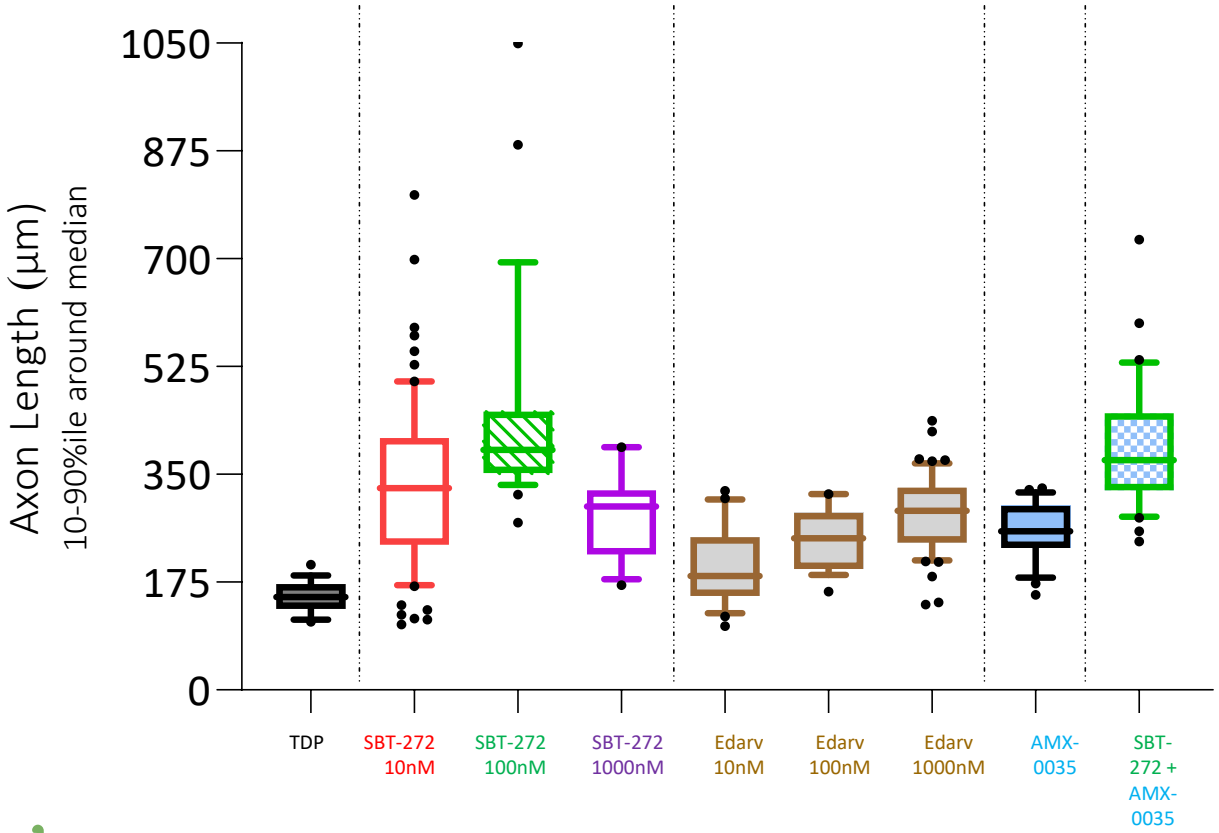


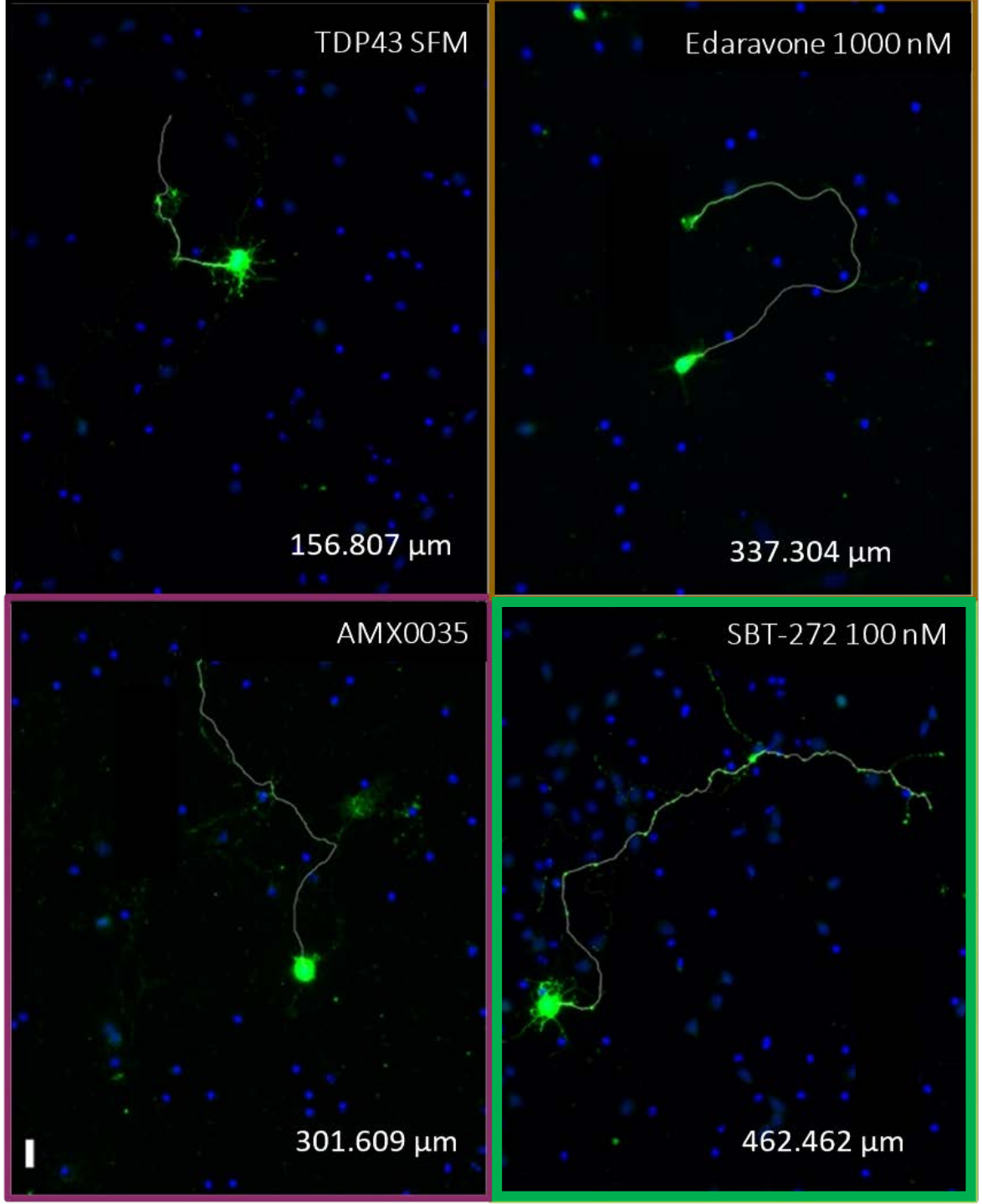


Stealth BIOTHERAPEUTICS

SBT-272 Shows Benefit Over Other Approved Therapies

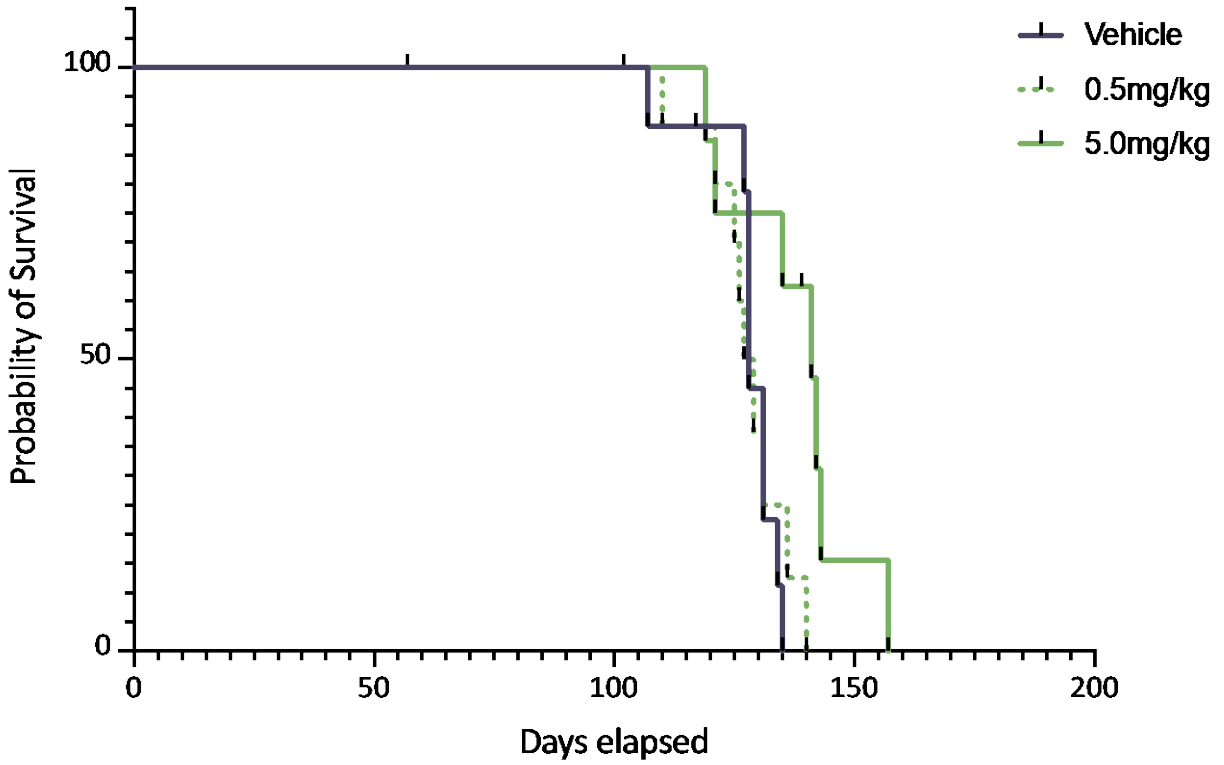
SBT-272 Improves Axonal Length Relative to Edaravone & AMX-0035 in ALS In Vitro Model





Gautam, Ozdinler *et al*, submitted 2022

SBT-272 Improves Survival in a Mouse Model of ALS



High copy number SOD1 G93A transgenic with 10 M & 10 F per group
Daily IP dosing starting @P56
Weekly neurological scoring

Bi-weekly grip strength
Bi-weekly blood draws
Plasma exposure in females was lower than in males

Phase 1 Dosing Completed; 2023 IND Submission Planned

Chronic Toxicology Studies Ongoing to Inform Potential 2024 P2 Initiation

2022

- Conducted Phase 1 study of single and multiple ascending dose of SBT-272 in healthy volunteers
- Initiated chronic toxicology studies in 2 species
- Orphan drug designation granted by US FDA

2023

- IND submission planned

2024

- Planned initiation of Phase 2 clinical trial in patients with ALS

Stealth BIOTHERAPEUTICS

MITO is Leading Mitochondrial Medicine

Clinical Stage Company with Deep Pipeline of Novel Compounds Targeting Genetic and Age-related Diseases

Leading mitochondrial medicine

- **Genetic diseases:** nPMM (clinical), Barth (clinical), Friedreich's (clinical), Duchenne (pre-IND), ALS (preclinical)
- **Age-related diseases:** GA (clinical), glaucoma (preclinical)

Significant unmet need

- **Genetic diseases:** ~7,000 US nPMM, <200 US Barth, ~7,000 Friedrich's, ~12,000 US Duchenne, ~16,000 US ALS
- **Age-related diseases:** ~2m US AMD

First in class therapies

- **Fast track:** nPMM, Barth, LHON, GA
- **Orphan drug:** nPMM, Barth, FRDA, 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**

Near-term milestones may drive significant value inflection.

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