Second Quarter 2021 Financial Results Earnings Call

Stealth BIOTHERAPEUTICS

Leading Mitochondrial Medicine

August 5, 2021

Second Quarter 2021 Earnings Call

Forward Looking Statements

- **HENRY HESS,** *Chief Legal Counsel*

Introduction and Business Highlights

- **REENIE MCCARTHY,** *Chief Executive Officer*

Update on Pipeline Programs

- **JIM CARR,** *Chief Clinical Development Officer*
- **BRIAN BLAKEY,** *Chief Business Officer*
- **MARTY REDMON,** *Chief R & D Officer*

Financial Results Q2 2021

- **ROB WEISKOPF,** *Chief Financial Officer*

Questions & Answers

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 our plans, strategies and expectations for our preclinical and clinical advancement of our drug development programs, including our ongoing clinical trials of elamipretide and planned clinical trial of SBT-272; our plans for the potential submission of an NDA for Barth Syndrome; our expectations regarding regulatory interactions, including our belief that the existing data may provide sufficient evidence to support NDA review; the potential benefits of our product candidates; our key milestones for 2021 and 2022; our plans regarding future data presentations; and our financial guidance regarding the period in which we will have capital available to fund our operations. Statements that are not historical facts, including statements about our 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. We 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: our 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 our product candidates and future product candidates; the preclinical and clinical results for our product candidates, which may not support further development and marketing approval; the potential advantages of our 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 our product candidates; our ability to obtain and maintain requisite regulatory approvals and to enroll patients in our planned clinical trials; unplanned cash requirements and expenditures; competitive factors; our ability to obtain, maintain and enforce patent and other intellectual property protection for any product candidates we are developing; and general economic and market conditions. These and other risks are described in greater detail under the caption "Risk Factors" included in our 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, we do not undertake any obligation to update forward-looking statements made by us to reflect subsequent events or circumstances.

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STRATEGY

CARDIOLOGY PLATFORM
Reverse remodeling the failing heart

OPHTHALMOLOGY PLATFORM
Improving vision in blinding diseases

NEUROLOGY PLATFORM
Evidence of peripheral improvements; early signs of neuronal protection

2021 KEY MILESTONES

BARTH NDA SUBMISSION *expected August 2021. FDA feedback received on Friedreich's protocol. Ongoing efforts to initiate up to 2 additional indications.*

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FDA ALIGNED ON PHASE 3 TRIAL IN nPMD *expected to initiate by year-end. Continued promising data and progress with next-generation clinical stage compound SBT-272.*

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CARDIOLOGY PLATFORM

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Barth: Regulatory Discussions Regarding Evidence of Effectiveness

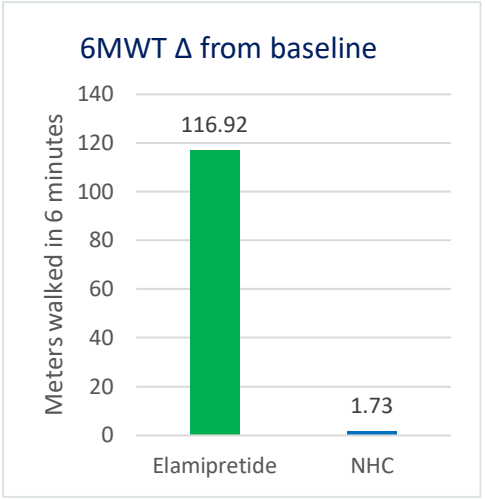
Division of Neurology Products (DNP) 2016 - 2019	• 2019: Recommended conduct of randomized withdrawal trial enrolling 8 OLE patients. • 2019: IND transferred to DGIEP.
Division of Gastroenterology & Inborn Errors of Metabolism Products (DGIEP) 2019	• 2019: Reiterated DNP advice; did not agree to an external control but provided feedback on one in the SPIBA-001 protocol. • 2019: IND transferred to DRDMG.
Division of Rare Disease & Medical Genetics Products (DRDMG) 2020	• 2020: Reiterated DNP advice regarding generation of additional data, which could be by withdrawing patients in OLE.
Division of Cardiology & Nephrology (DCN) 2020 - 2021	• 2020 pre-IND meeting (regarding Barth cardiomyopathy); IND transferred to DCN in 2021. • February 2021: noting infeasibility of new study, DCN advised SBT to submit its NDA. • March/April 2021: reversed prior guidance; advised that more data should be generated which could be by a randomized withdrawal trial utilizing OLE patients and additional patients. • June 2021: responded to pre-NDA questions related to formatting and presentation of data; reversed prior guidance and advised that no informative data could be obtained with randomized withdrawal trial; approved Barth intermediate expanded access protocol.

SPIBA-001 Phase 3 Natural History Control Study + Supportive Data

SPIBA-001 Phase 3 Data (summary)

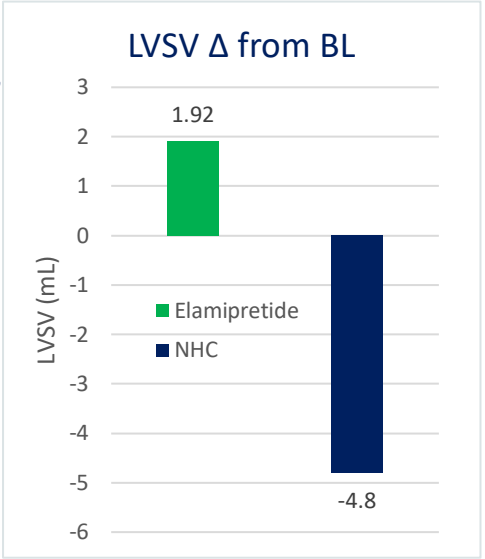
- Primary endpoint 6MWT improved over NHC by
  - **79.7** meters after 36-weeks (p=0.0004)
  - **90.97** meters after 48-weeks (p=0.0005)
  - **115.19** meters after 72-weeks (p=0.0003)
- All secondary endpoints (Muscle strength, 5XSST, balance and a multi-domain responder index) improved over NHC and all were significant after 72-weeks.
- Improvement in left ventricular stroke volume (p=0.002) is not expected by the NH, where this parameter continues to decline in boys ≥12-years-old

*Week 72 analysis conducted post-hoc at FDA request



Week 72 OLE: p=0.0003

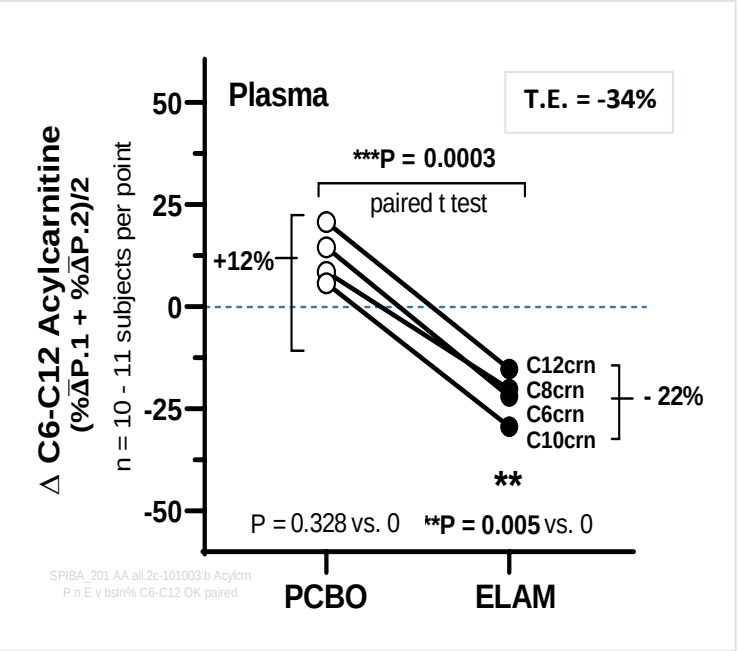
Week 36 OLE: Elam 80.30, NHC 0.60, p=0.0004
Week 48 OLE: Elam 91.86, NHC 0.89, p=0.0005



Week 72 OLE: LSM 6.72, p=0.002

Supportive Data from SPIBA-201 Part 1

- **Reductions in Prognostic Markers of Cardiac Dysfunction:** *Reduced* medium-chain (C_6-C_{12}) acylcarnitines (AC) p=0.005



- Echocardiographic parameters improved for 10/12 subjects

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

Accelerated approval pathway

FDA Perspective

"This pathway is available under federal law when a drug intended for a serious disease is expected to provide a meaningful advantage over available treatments. A drug may be approved under this pathway when it is shown to improve a measure of a disease and when it is "reasonably likely" that this measure predicts clinical benefit. Note that the law says "reasonably likely" to predict, not "certain" to predict. In other words, accelerated approval was designed for situations in which there is residual uncertainty about clinical benefit."

Drs. Cavazzoni, Dunn and Stein
Washington Post Opinion 6/23/2021

Proposed Surrogate and Interim Clinical Endpoints for Barth

- **Left ventricular stroke volume:** declines in NH; improves with elamipretide; improvements increasingly correlated to clinical benefit (improvement in exercise tolerance) as has also been demonstrated in other relevant pathologies
- **Acylcarnitines:** prognostic markers of cardiac dysfunction known to be elevated in Barth and other forms of HF; declines with elamipretide relative to placebo
- **MLCL:CL ratio:** elevations are pathophysiological basis of disease and diagnostic for Barth; declines following elamipretide for all exposed patients
- **6MWT:** itself a clinical endpoint, it may also be an interim clinical endpoint reasonably likely to predict long term reversal of morbidity (exercise intolerance, fatigue, potentially mortality) in Barth; improves with elamipretide; improvements correlated with cardiac improvements and not due to increased effort

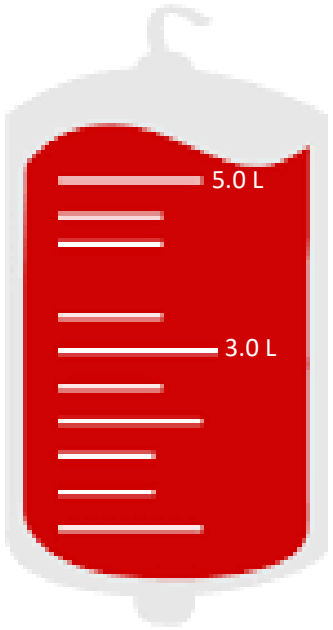
Fatima et al., Metabolites, 2019; Kuka et al., Sci Rprts, 2017; Oates Poster BTHS SMS 2020.

Stroke volume is reasonably likely to predict clinical benefit

SV is a key component of CO and EF. All forms of HF are associated with deteriorating SV and CO; EF has been well-correlated with survival.

SPIBA-201 patients under-perfused at BL

mean BL CI = 2.3L/min/m^2 (~3,300 L/day)



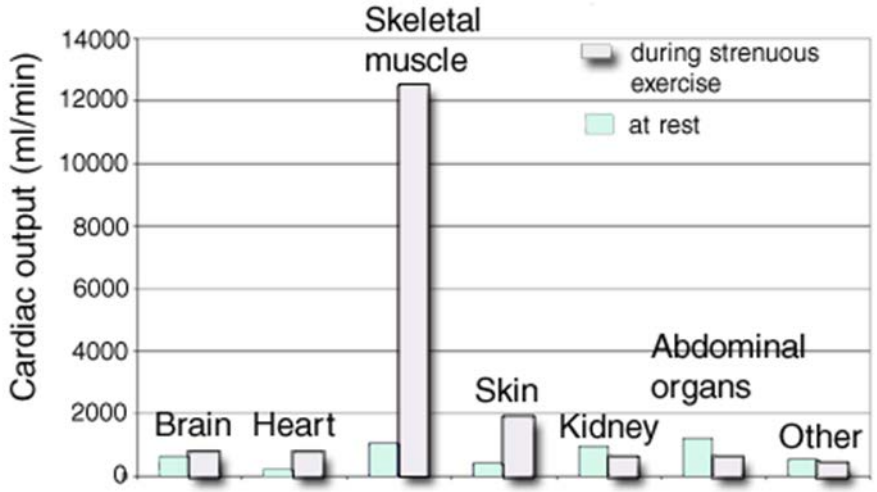
Healthy teenager
~4.13L/min/m2
(6,000-7,500 L/day)

Congestive heart failure
~2.3L/min/m2

Cardiogenic shock
<2.2L/min/m2

CO = cardiac output, the amount of blood pumped each minute (SV X HR)
CI = cardiac index (CO indexed to body surface area)
EF = % of blood in left ventricle ejected with each contraction (EF = SV/EDV)
HR = heart rate
SV = stroke volume

Cardiac Output, Particularly During Exercise, is Crucial for Muscle Performance



- Elamipretide-mediated improvements in SV were increasingly correlated with improvements in exercise (r=0.64 at W72 OLE), establishing that it is reasonably likely to predict improvements in the progressive myopathy in Barth
- The predictive benefit of SV on exercise tolerance has been demonstrated in other cardio-pulmonary disorders

Morantz, Am. Fam. Phys., 2003; Cattermole, Phys. Reps., 2017; Carsson et al., J Cardiovasc Magn Reson. 2012; Klabunde, Card. Phys. Conc., 2012 ACC Poster Presentation, 2020; Berliner et al Eur J Cardiothorac Surg. 2019; Lele et al., 1995; . http://www.medicine.mcgill.ca/physio/vlab/exercise/cardio_cns.htm

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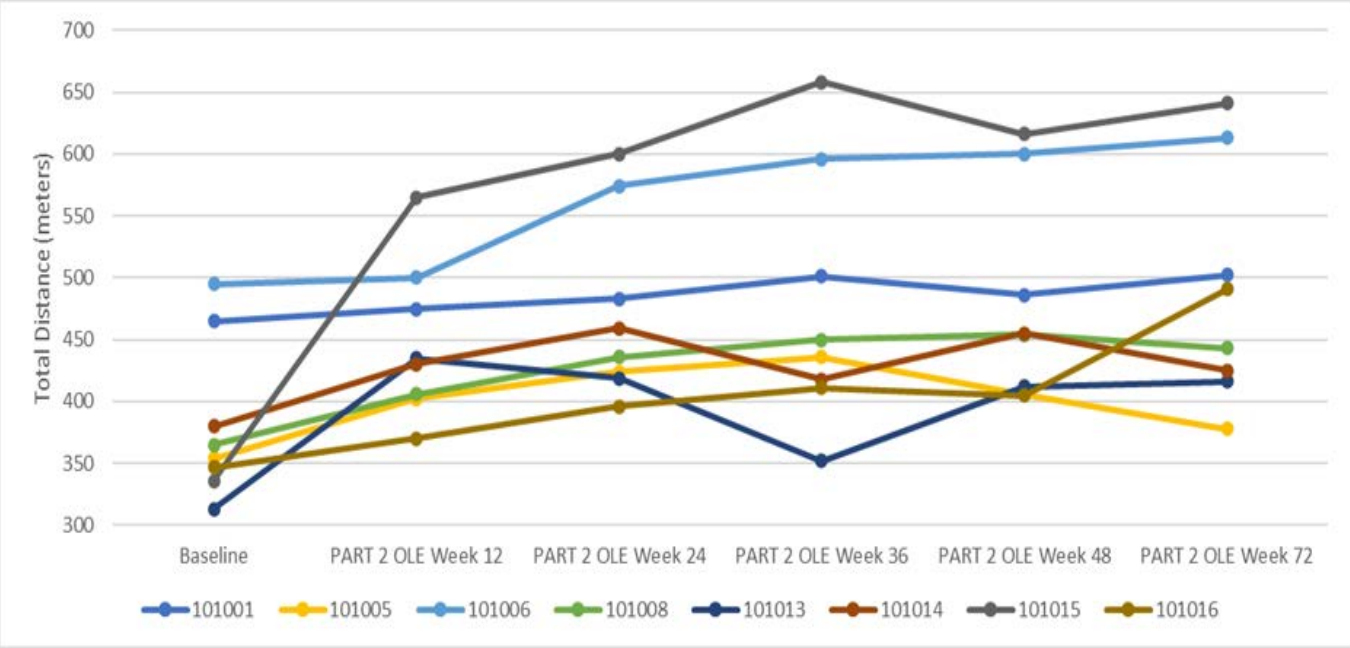
6MWT as an intermediate clinical endpoint

[A]n intermediate clinical endpoint is a measure of a therapeutic effect that is considered reasonably likely to predict the clinical benefit of a drug, such as an effect on irreversible morbidity and mortality.

https://www.fda.gov/patients/fast-track-breakthrough-therapy-accelerated-approval-priority-review/accelerated-approval

6MWT Subjects Enrolled in SPIBA-201 OLE through Week 72



SPIBA-201 OLE

>100-meter mean improvement in 6MWT (~25% improvement over baseline)

durable >2 years

exceeds reported effects of other approved HF agents[1]

correlated with cardiac improvements(r=0.52)

unbiased no observed increase in effort from Part 1 baseline through OLE Week 72

The improvements in 6MWT are considered reasonably likely to predict elamipretide's effect on the irreversible morbidity of Barth, where skeletal myopathy is progressive over time and becomes severe by the fourth decade of life.

Barth Voice of the Patient Report

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

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Mechanistic reasoning: MLCL:CL ratio

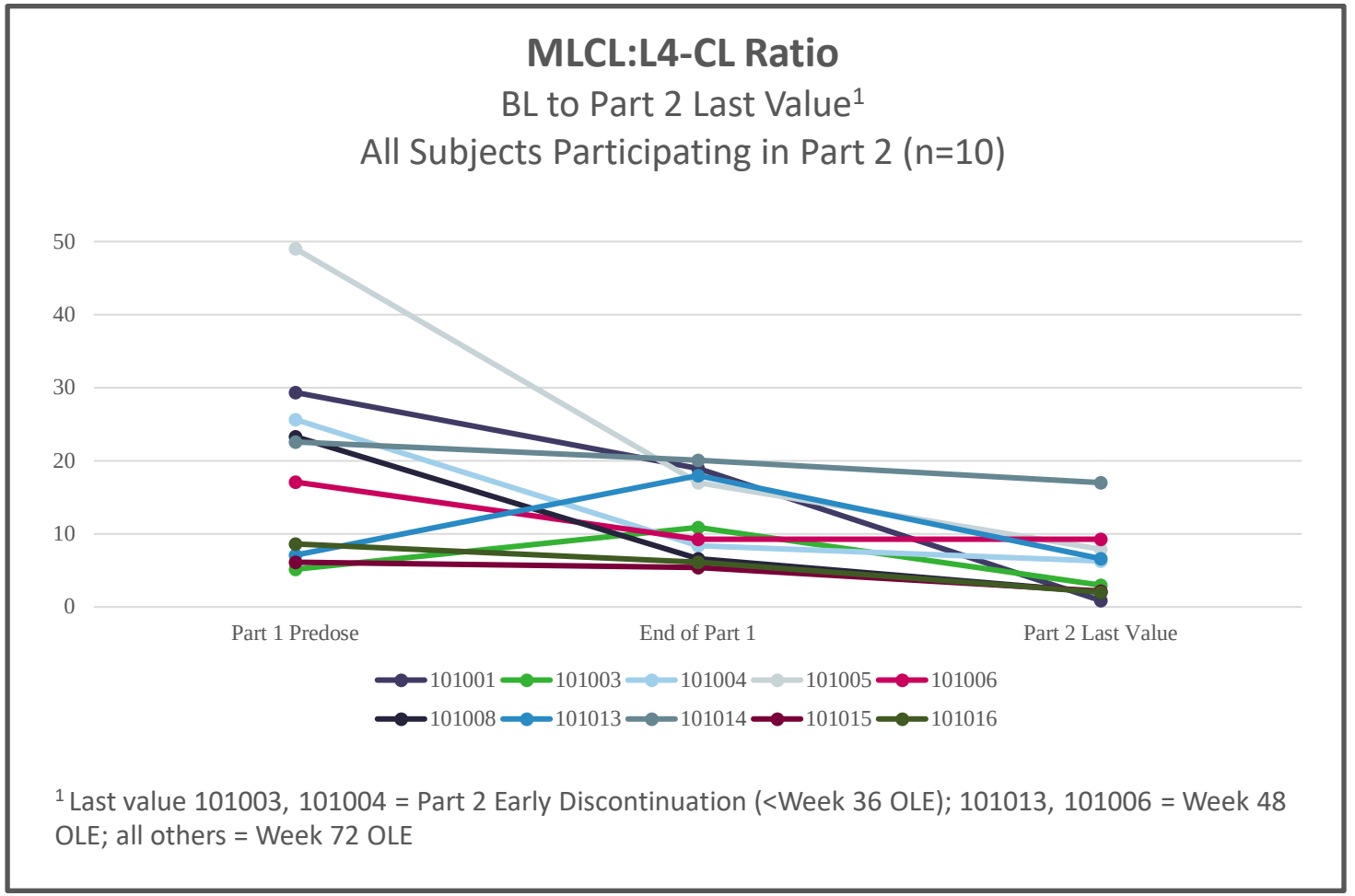
FDA Perspective

"It's becoming more and more of a problem. The FDA or anybody who's industry can't just look people in the face and say, well, you have an ultra-rare disease, abandoned all hope and we'll never get any treatments for you...

Ultra-rare diseases are "a place where mechanistic reasoning may really play a major role."

"The 50-year investment in basic science has to merge with clinical methodology and we have to stop just thinking that empirical evaluation is the only way of determining truth."

Pink Sheet quoting Acting Commissioner Woodcock; Ultra-Rare Disease Approvals by US FDA Could Take More 'Mechanistic,' Less 'Empirical' Approach; 7/1/2012



[1] Last value 101003, 101004 = Part 2 Early Discontinuation (<Week 36 OLE); 101013, 101006 = Week 48 OLE; all others = Week 72 OLE

Every subject's MLCL:CL ratio improved from first to last visit; significant improvement by W72 OLE

Tolerance for less certainty of benefit

FDA Perspective

Why would we accept uncertainty when approving a drug? The accelerated pathway was created to give earlier access to potentially valuable drugs for patients who have a serious disease…with limited or no treatment options. These patients are often willing to accept some degree of uncertainty of clinical benefit.

Drs. Cavazzoni, Dunn and Stein
Washington Post Opinion 6/23/2021

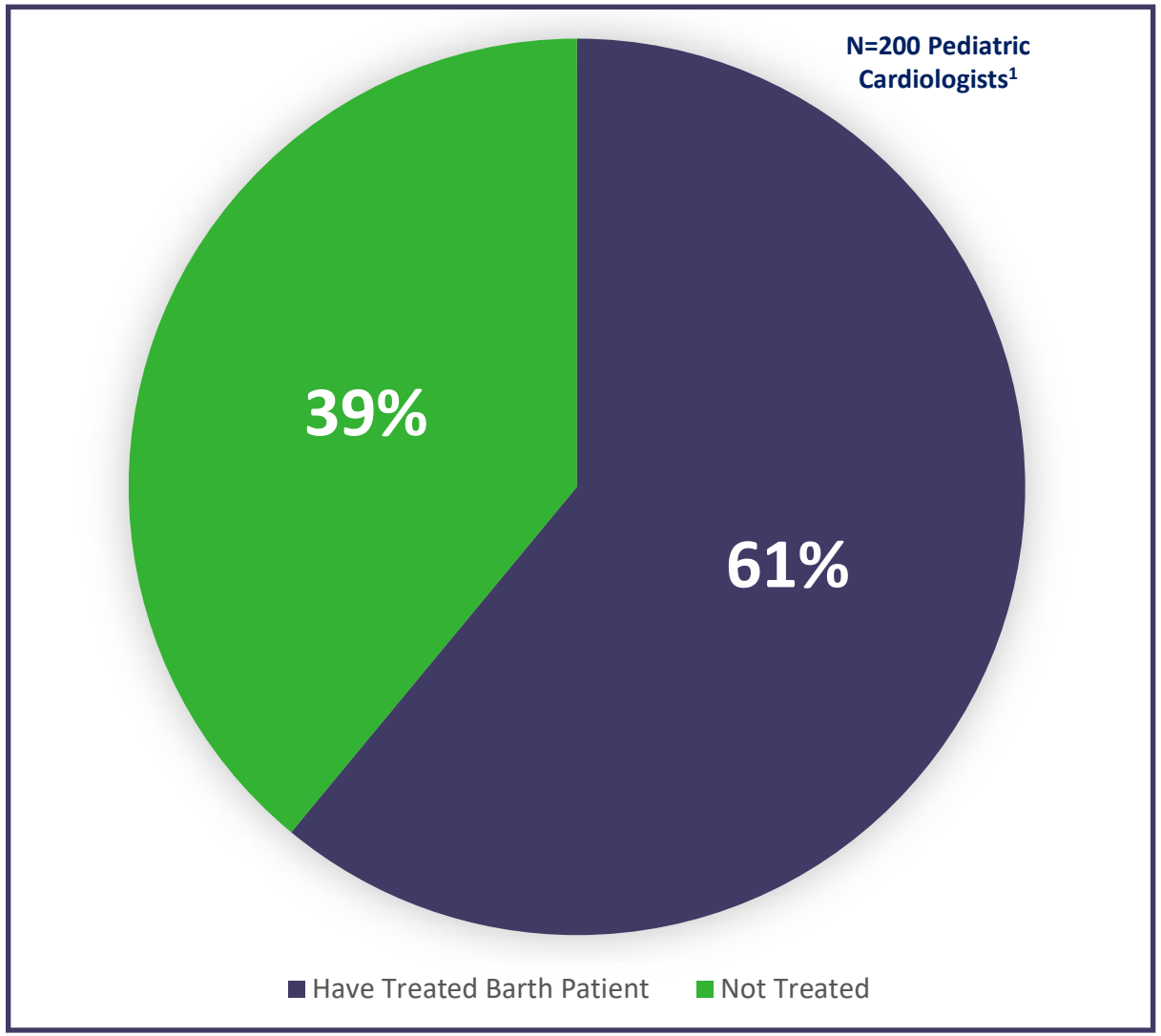
Themes from 3/31/2021 BSF-FDA Listening Session regarding uncertainty of benefit

- Barth syndrome itself means living with constant uncertainty.
- No clinical benefit is ever guaranteed, but patients want to have the option to try something that provides some chance of benefit.
- The need for a treatment sooner, even if it comes with greater uncertainty, is warranted because day-to-day quality of life really matters.
- Patients and caregivers would be willing to try a drug that might result in an improved quality of life even if the benefit is uncertain or, notably, even when it might be at the expense of a longer life.
- If progress is going to be made toward treatments for Barth syndrome, we must participate in research.
- There is risk in NOT trying a new possible treatment
- The ultimate decision to participate in a trial or to try a new treatment would involve individual risk/benefit analysis that would depend on the particulars of the patient's age and condition.

"The need is great. With an ultra-rare disease like BTHS, there will never be a high degree of confidence as to whether a treatment works or doesn't work. If there is sufficient evidence that a drug is relatively safe, we need to allow patients and their families the ability to choose to try something."

https://www.barthsyndrome.org/advocacy/fda-listening-session.html

Broadening Awareness of Unmet Need in Barth



[1] Bruno and Ridgway Research Associated, April 2021, Survey of 200 Pediatric Cardiologists

Publications and Presentations Support the Potential of Elamipretide as the First Treatment for Barth

nature genetics

A phase 2/3 randomized clinical trial followed by an open-label extension to evaluate the effectiveness of elamipretide in Barth syndrome, a genetic disorder of mitochondrial cardiolipin metabolism

ASHG American Society of Human Genetics

Elamipretide Significantly Improves Disease Symptomatology versus Natural History Controls in Barth Syndrome

AMERICAN COLLEGE of CARDIOLOGY

Elamipretide Improves Functional Assessments when Compared to the Natural History Progression of Cardiomyopathy-related Disease Symptomology in Patients with Barth Syndrome

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NEUROLOGY PLATFORM

2021 KEY MILESTONES

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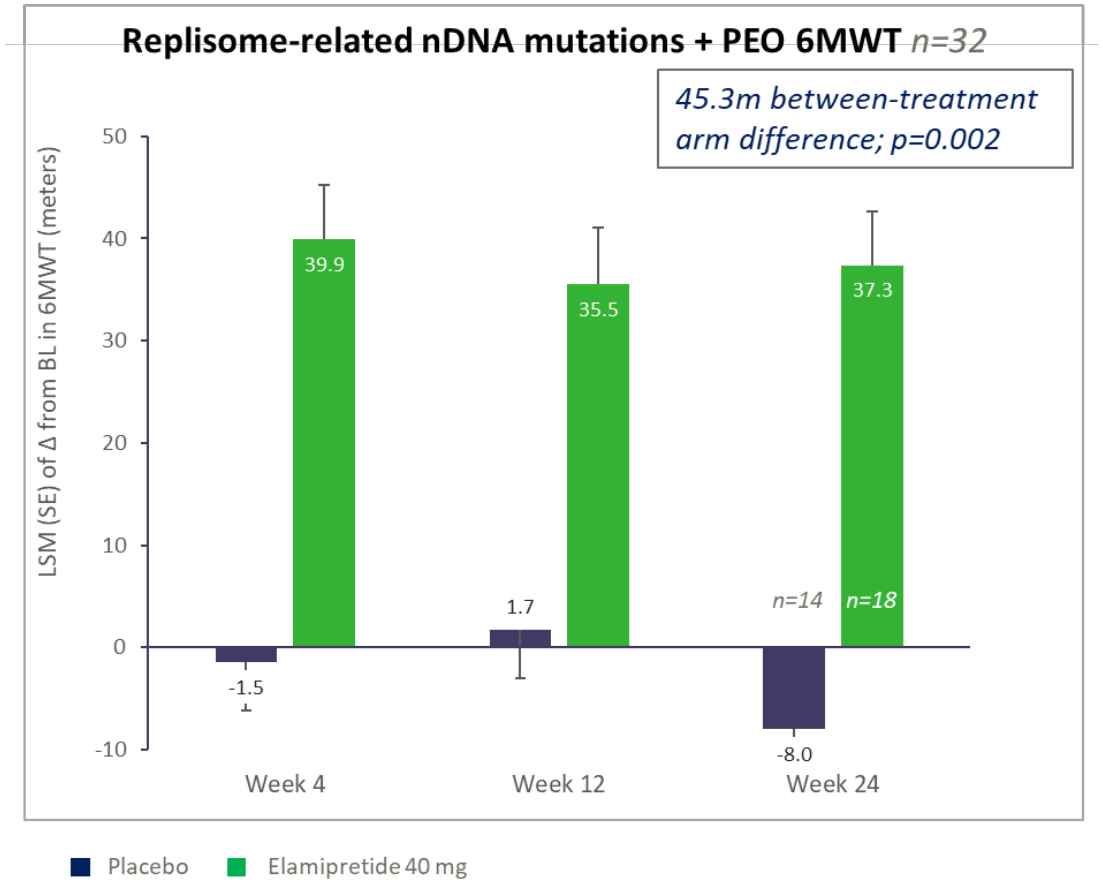
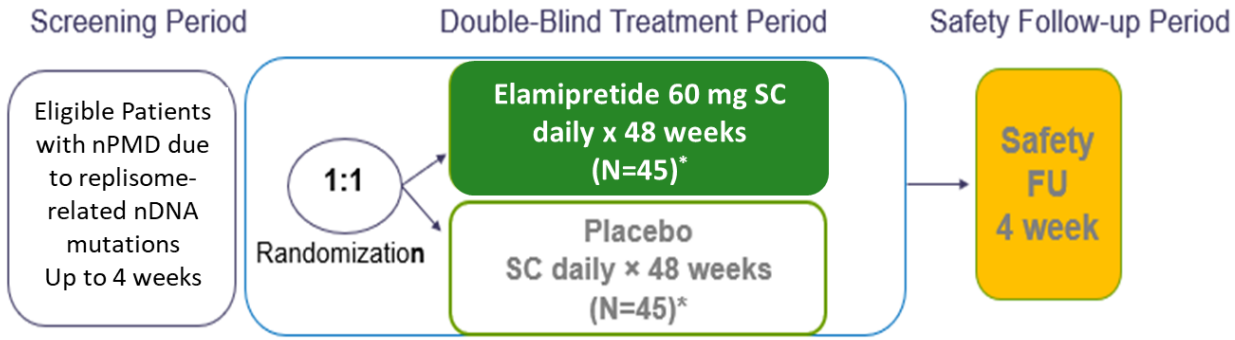
Phase 3 initiation by year-end 2021

SPIMM-301 Patients Eligible for new P3 inclusion



Aligned w/FDA on P3 trial design, rationale



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

- Enrich for patients most likely to respond (= the primary analysis group)
- Increased dose due to significant exposure-response relationship observed

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CARDIOLOGY PLATFORM

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Friedreich's ataxia

Screening

Genetically confirmed FRDA	n=16
Primarily visually compromised: Visual acuity worse than 20/40 Impaired contrast: • high contrast visual acuity of 20/50-20/800, or • hand motion vision	Primarily affected by cardiac dysfunction: • Ejection fraction <50% and • Visual acuity of 20/25-20/40

BL W1 W4 W16 W36 W52 | **Optional 52-week extension**

Interim analysis

8 = Elamipretide 30 mg (s.c.)

Compared to

8 = Elamipretide 60 mg (s.c.)

Once daily

May be extended to 2-year duration to assess durability of any observed response

Safety Endpoints
Adverse event attributed to drug

Ophthalmic Efficacy Endpoints
High contrast visual acuity or low vision alternative
Low contrast visual acuity
Low luminance visual acuity (LLVA)
Optical coherence tomography
Visual function questionnaire

Cardiac Efficacy Endpoints
Ejection fraction by cardiac MRI
Left ventricular volume index
Stroke volume
Fibrosis
Strain

Exploratory Efficacy Endpoints
MFARS, FA ADL, FA functional disability scale
REDENLAB speech assessments
PGIC/CGIC

* Protocol subject to IRB approval

*protocol changes in response to Division of Ophthalmology comments on protocol

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OPHTHALMOLOGY PLATFORM

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Mitochondrial dysfunction precedes vision loss, correlates with potential to improve visual function in dry AMD

ReCLAIM High Risk Drusen Cohort (n=21)	ReCLAIM Geographic Atrophy Cohort (n=19)

Changes in low light visual acuity were correlated with baseline mitochondria-rich ellipsoid zone (EZ) health measured by:

- Mean central macular (e.g., central 2 mm) retinal thickness (r = 0.58; *p* = 0.009)
- % of EZ attenuation (r = -0.72; *p* = 0.002)
- EZ retinal pigment endothelial cell volume (r = 0.62; *p* = 0.01)

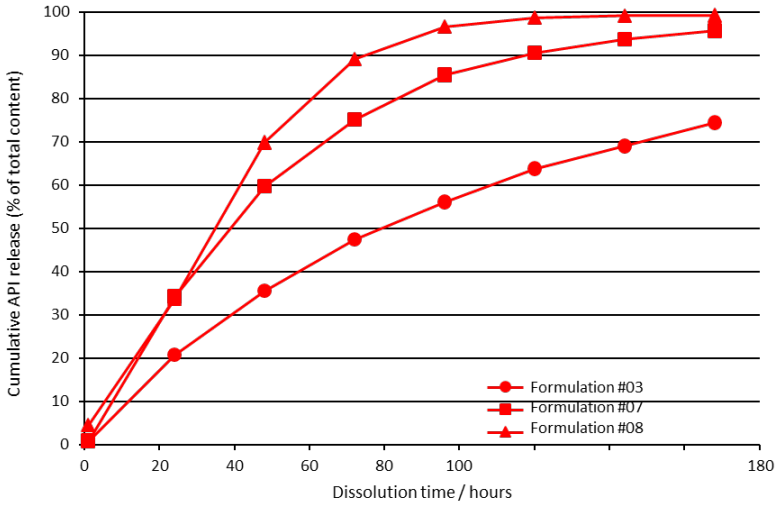
Earlier treatment may lead to improved outcomes, with eyes gaining ≥2-lines of low light visual acuity having:

- Greater baseline preservation of the central macular outer retina (ONL-RPE thickness, 137 µm vs 117 µm; *p* = 0.006)
- Trend towards less baseline macular partial EZ attenuation (1.1% vs 5.0%; *p* = 0.06)
- Less EZ attenuation at baseline (9.0% vs 27%; *p* = 0.03)
- Less % area of macular geographic atrophy (4.7% vs 15.6%; *p* = 0.004)

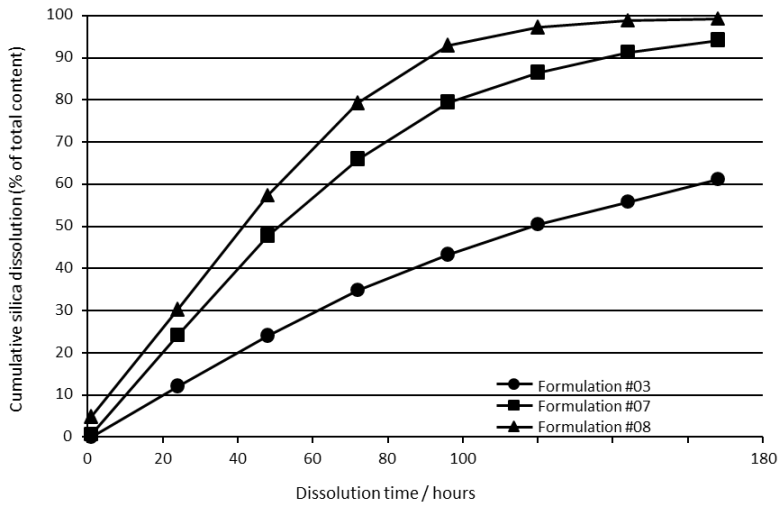
IVT development ongoing

Feasibility Stage

Drug release mimics matrix dissolution, anticipated 4-10 month release.



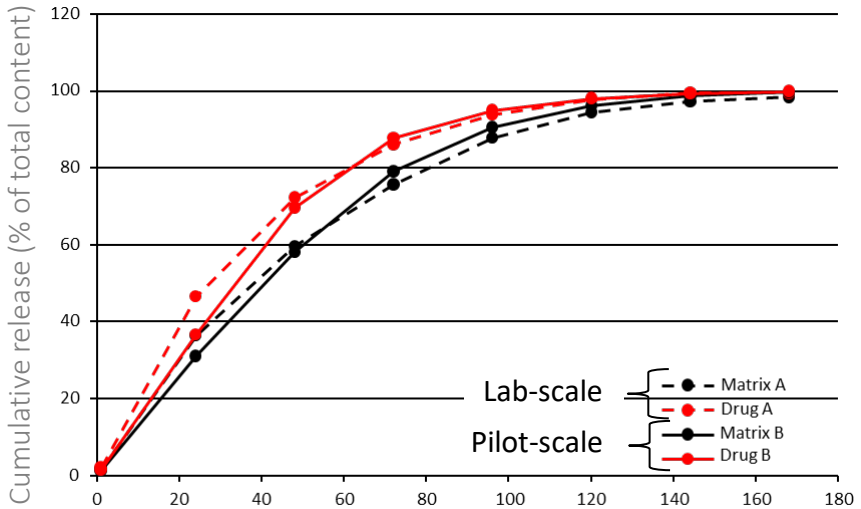
Drug release



Matrix dissolution

In Vitro Release Testing

Drug release mimics matrix dissolution



Plan to complete *in vitro* efficacy, retinal PK & IVT drug product ready for GLP tox testing commensurate with ReCLAIM-2 data.

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NEUROLOGY PLATFORM

2021 KEY MILESTONES

ENROLL BARTH PHASE 3 RANDOMIZED WITHDRAWAL TRIAL *to support 2022 NDA submission, progress European regulatory initiatives and progress initiation of up to 3 additional indications*

REPORT PHASE 2 GA RESULTS IN EARLY 2022 *with Phase 2 demographics and additional Phase 1 data during 2021 to support potential to reclaim visual function; IVT feasibility ongoing*

INITIATE PHASE 3 TRIAL IN nPMD *whilst progressing next-generation clinical stage compound SBT-272 to Phase 2 readiness*

Second Quarter 2021 Financial Results

(In Millions)	Three Months Ending June 30	
	2021	2020
Total Revenue	-	-
Total Operating Expenses		
Research and Development	5.9	7.4
General and Administrative	5.1	4.5
Net Loss from Operations	11.0	11.9

We expect our cash and cash equivalents of $30.76 million as of June 30, 2021 and the $27.0 million of additional funding under the Development Agreement expected during 2021 to fund our operations into the second quarter of 2022

Building a Transformational Foundation for Mitochondrial Medicine

2021

- Submit Barth NDA
- Start Phase 2a Investigator-Sponsored Clinical Trial in Friedreich's Ataxia
- Initiate Regulatory Engagements Ahead of Duchenne Cardiomyopathy Trial Initiation
- Prepare for ReCLAIM Phase 2 Read-out by Elucidating Enrichment Strategies and IVT Feasibility
- Start Phase 3 Clinical Trial in Primary Mitochondrial Disease due to nDNA Mutations
- Progress Toward Phase 2 Readiness for SBT-272 Neurology Indication(s)