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Zacks Small-Cap Research

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Stealth Biotherapeutics (MITO-NASDAQ)

MITO: A company pursuing mitochondrial research to solve currently unsolvable medical issues.

MITO is clinical stage biopharmaceutical company that is attempting to repair mitochondria to treat previously untreatable conditions. We place a $2.10 valuation on MITO using a discounted cash flow model.

Current Price (02/22/22)	$0.49
Valuation	**$2.10**

OUTLOOK

Stealth BioTherapeutics is using ground-breaking research to repair damaged mitochondria, located in almost all cells and producing energy and performing other crucial functions, in an effort to treat currently diseases with now current treatments.

The company has its signature treatment, elamipretide, in the FDA approval process for various conditions, including: Barth Syndrome, dry AMD and Duchenne Muscular Dystrophy.

SUMMARY DATA

52-Week High	**$2.18**
52-Week Low	**$0.62**
One-Year Return (%)	**-71.15**
Beta	**1.81**
Average Daily Volume (sh)	**62,482**
Shares Outstanding (mil)	**58**
Market Capitalization ($mil)	**$28**
Short Interest Ratio (days)	**N/A**
Institutional Ownership (%)	**2**
Insider Ownership (%)	**N/A**
Annual Cash Dividend	**$0.00**
Dividend Yield (%)	**0.00**
5-Yr. Historical Growth Rates	
Sales (%)	**N/A**
Earnings Per Share (%)	**N/A**
Dividend (%)	**N/A**
P/E using TTM EPS	**N/A**
P/E using 2022 Estimate	**-8.9**
P/E using 2023 Estimate	**N/A**
Zacks Rank	**N/A**

Risk Level	**High**
Type of Stock	**N/A**
Industry	**N/A**

ZACKS ESTIMATES

Revenue
(in millions of $)

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2021	0.0 A	0.0 A	0.0 A	0.0 E	0.0 E
2022	0.0 E	0.0 E	0.0 E	0.0 E	0.0 E
2023	0.0 E	0.0 E	0.0 E	0.0 E	0.0 E
2024	0.0 E	0.0 E	0.0 E	0.0 E	0.0 E

Earnings per share

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2021	-$0.01 A	-$0.03 A	-$0.01 A	-$0.02 E	-$0.07 E
2022	-$0.02 E	-$0.03 E	-$0.01 E	-$0.01 E	-$0.07 E
2023	-$0.01 E	-$0.02 E	-$0.02 E	-$0.01 E	-$0.06 E
2024	-$0.02 E	-$0.01 E	-$0.01 E	-$0.02 E	-$0.06 E

INITIATING COVERAGE

We are initiating coverage of Stealth Biotherapeutics (MITO) with an initial valuation of $2.10. Stealth Biotherapeutics is a clinical-stage biopharmaceutical company based in Massachusetts but incorporated in the Cayman Islands that is developing therapies to treat mitochondrial dysfunction associated with genetic mitochondrial disease and many age-related diseases.
Mitochondria is an organelle found in large numbers in most cells, in which the biomechanical processes of respiration and energy production occur. Mitochondria are a relatively recent addition to the scientific community with regard to disease recognition with molecular biology and the discovery of pathogenic mitochondrial DNA defects occurring in the 1980s. Since then, scientists and researchers have been pursuing ways to positively impact those mitochondrial defects in an effort to relieve patient suffering. While we have seen much excitement and potentially exciting developments surrounding mitochondria and their ability to be positively manipulated, the reality, in our view, has been somewhat less than inspiring to this point, with very few treatments actually coming to fruition. Stealth Biotherapeutics is aiming to break through that malaise and is pursuing multiple courses in an effort to bring relief to patients who, to this point, have little-to-no hope for any longer-term answer.

The primary candidate from Stealth to make this breakthrough is with a compound called elamipretide. This is going to get into the mitochondrial weeds a bit and will be expounded on further in the report, but elamipretide is a peptide compound that readily penetrates cell membranes and targets the inner mitochondrial membrane where it binds reversibly to cardiolipin. Elamipretide is being investigated in the treatments of various conditions, including:

- Barth Syndrome
- Duchenne Muscular Dystrophy (DMD)
- Friedreich's Ataxia (FRDA)
- Dry Age-Related Macular Degeneration
- Leber's Hereditary Optic Neuropathy (LHON)
- Neuromuscular nDNA-related Primary Mitochondrial Myopathy

We will discuss the above conditions further below but suffice it to say that these are conditions where there are no current approved treatments and several of which Stealth has received Fast Track and Orphan Drug designations from the FDA.

Stealth had a recent infusion of capital—toward the end of 2021—that management has said gives them the funding needed to fund operations through the third quarter of 2022. Obviously, the company is going to require more funding, but that recent infusion gives them a little breathing room before having to go back to the capital markets.

THE SCIENTIFIC STORY

Stealth BioTherapeutics is operating in a space, in our view, that is informed by extensive research, that has an abundance of opportunity but also an abundance of uncertainty. We are encouraged by what we view as a solid team established by Stealth in pursuing these goals as well as the progress the company has made toward bringing therapies to market. Additionally, Stealth's leading compound candidate, elamipretide, has been reported to well tolerated in clinical trials of over 1,000 subjects systemically exposed to it to date, with some having exposure to the drug for over four years. And elamipretide, along with a couple of other compounds being investigated, are fairly far along in the approval process, shown in the table below, which adds to the encouragement we have regarding Stealth's prospects.

Stealth BioTherapeutics 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		

Source: www.stealthbt.com--February 16, 2022

As mentioned above, however, the promise of mitochondrial research has not been met with reality to this point, and Stealth is trying to break through barrier from the promise to realization. Therefore, the next couple of years will be critical for Stealth, in our view, for the company can bring one or more of these therapies across the finish line and to commercialization or developing a lucrative partnership with a larger drug company, while also maintaining the funding level needed to do so. Part of the challenge facing Stealth is in finding patients to conduct clinical trials for several of the conditions the company is investigating due to the limited number of people afflicted with conditions such as Barth Syndrome. But before we get into all of that, we need to go back to the beginning and take a deeper look at what mitochondria is and how it is structured in order to understand how Stealth's compounds may be the answer patients are looking for.

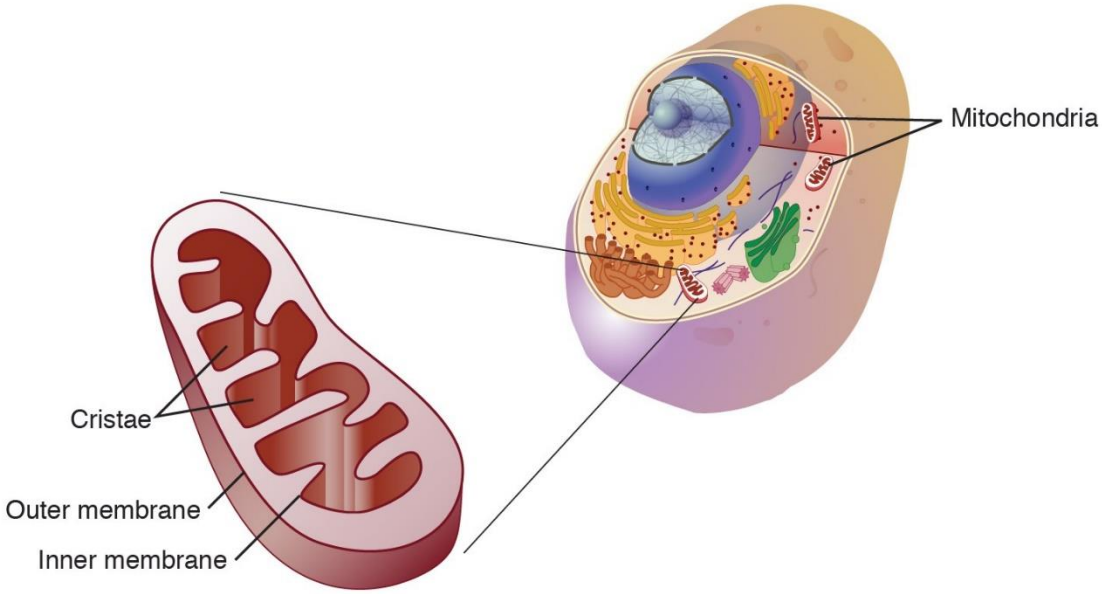
Mitochondria

Mitochondria, often described as the "powerhouse of the cell", are responsible for approximately 90% of energy production in human cells and are found in all human cells other than mature red blood cells. Mitochondria produce energy through the conversion of food into adenosine triphosphate (ATP). This happens through a series of reactions, controlled by the electron transport chain (ETC), within the inner folds of the mitochondria. The structure of mitochondria is broken down as follows:

- Outer membrane, which small molecules can pass through freely and includes proteins called porins, which form channels that allow proteins to cross. The outer membrane also contains various enzymes with a variety of functions.

- Inner membrane, which is impermeable to most molecules and holds proteins that have several roles. The inner membrane is where ATP is created.
- Cristae are the folds of the inner membrane and increase the surface area of the membrane, which increases the space available for chemical reactions.

Mitochondria Diagram



Source: Courtesy: National Human Genome Research Institute:https://www.genome.gov/genetics-glossary/Mitochondria

Different types of cells have differing numbers of mitochondria. Cells that have a high demand for energy tend to have greater number of mitochondria. As mentioned, mature red blood cells have none, liver cells can have more than 2,000 and around 40% of the cytoplasm in heart muscle cells is taken up by mitochondria. Although most human DNA is kept in the nucleus of a cell, mitochondria also contains its own set of DNA, known as mitochondrial DNA (mtDNA). Interestingly, although humans get half of their DNA from both their mother and father, as would be expected, mtDNA is received exclusively through the mother.

As mentioned above, mitochondria are known for their role in energy production but they also accomplish other vital tasks in the human body:

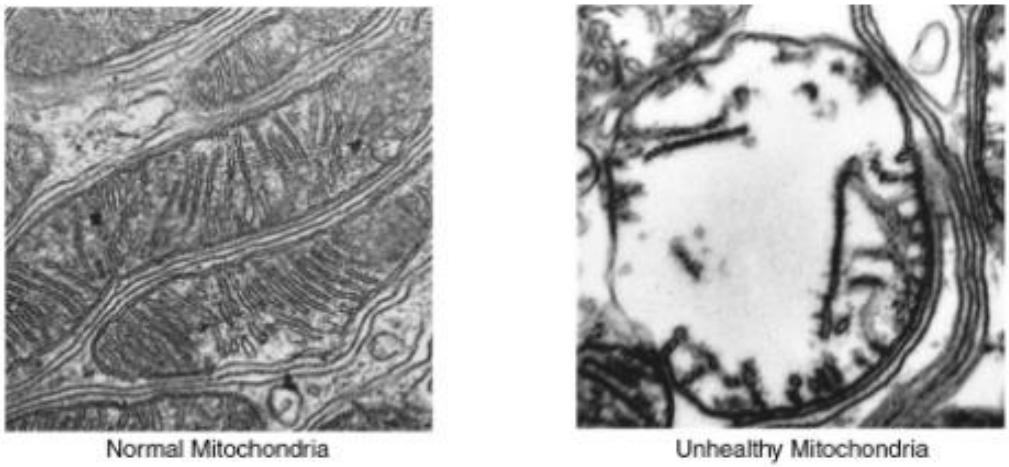
- Energy production mostly takes place on the cristae and chemical energy from food in converted into a form cells can use—a process known as oxidative phosphorylation.
- Cell death is an important part of human life as the body gets rid of old or broken cell and mitochondria is involved in the determination process of what cells get destroyed. Mitochondria release cytochrome C, which activates caspase, which is one of the main enzymes involved in the destruction of cells during a process known as apoptosis.
- Storing calcium, which is vital for cellular processes. Due to the importance of calcium, which is needed for muscle function, fertilization, and blood clotting for example, it is tightly regulated by cells. Mitochondria quickly absorb calcium ions and holds them until they are needed.
- Heat production through a tissue known as brown fat (found in its highest levels in babies), which produces non-shivering heat through a process known as proton leak.

Another important component of mitochondria is cardiolipin (CL). CL is a phospholipid exclusively located in the inner mitochondrial membrane and helps regulate various kinds of proteins such as

electron transport complexes, carrier proteins and phosphate kinases, and is essential in the organization of structures such as cristae.

When some of these processes are interrupted or disturbed through genetic abnormalities a person has dysfunctional mitochondria. Dysfunctional mitochondria can have an impaired ability to produce ATP and can generate increased levels of reactive oxygen species, or ROS, a major contributor to oxidative stress. Although low levels of ROS can be important signaling molecules in the cell, high levels of ROS can damage proteins and membrane lipids within the cell. Cardiolipin, in particular, is highly susceptible to oxidative damage, which can result in disrupted mitochondrial structure and a cycle of increasing ROS generation that can lead to the inflammation, fibrosis, senescence and cell death implicated in many human diseases.

Images of Healthy and Unhealthy Mitochondria



Normal Mitochondria | Unhealthy Mitochondria

Source: www.stealthbt.com--February 3, 2022

Mitochondrial dysfunction is commonly observed across both common and rare diseases. Contributors to mitochondrial dysfunction can include genetic mutations, the aging process, environmental factors, or a combination thereof. These impairments can affect a number of different organ systems, especially those with high energetic demands such as the heart, eyes, the brain, kidneys, and skeletal muscle.

Elamipretide

Stealth Biotherapeutics is focused on mitigating mitochondrial dysfunction in rare diseases such as primary mitochondrial myopathy due to nuclear DNA mutations (nPMM), Barth syndrome, and Duchenne muscular dystrophy, as well as a wide range of common age-related diseases, such as dry age-related macular degeneration.

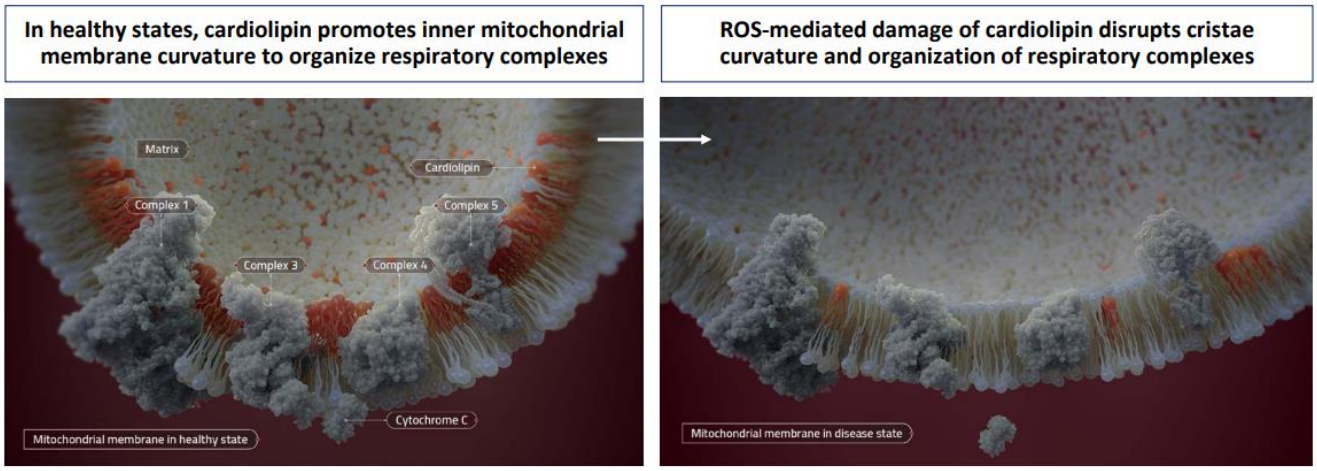
The company's current primary tool toward achieving those ambitious goals is elamipretide, which is Stealth's lead investigational product candidate. The company describes it as a "peptide compound that readily penetrates cell membranes and targets to inner mitochondrial membrane where it binds reversibly to cardiolipin."

Elamipretide is known to compensate for cardiolipin deficit by improving lipid packing, membrane curvature and membrane surface area. When brought into close proximity with the inner mitochondrial membrane, elamipretide's positively charged residues interact electrostatically with the anionic headgroups of cardiolipin, increasing local concentration levels.

Elamipretide's nonpolar side chains subsequently penetrate the inner mitochondrial membrane at gaps created by cardiolipin and interact hydrophobically with the acyl chains, depicted in the graphic

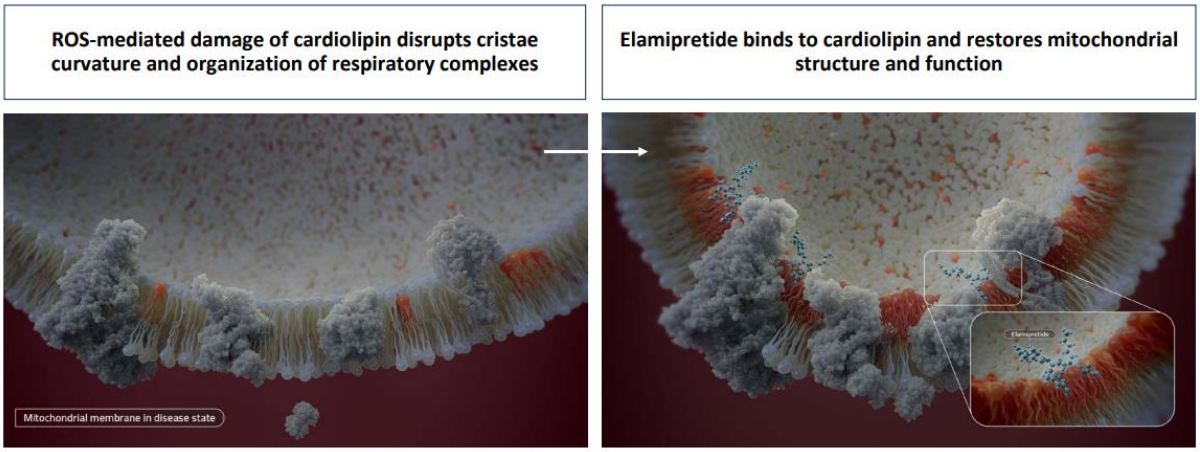
below. This electrostatic/hydrophobic binding modulates the surface electrostatics of the inner membrane to facilitate increases in lipid packing, membrane curvature and membrane surface area integral to cristae formation, supercomplex association and efficient oxidative phosphorylation.

Healthy and damaged cardiolipin



Source: www.stealthbt.com--February 3, 2022

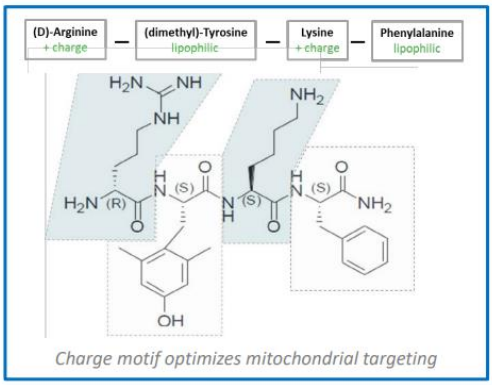
Elamipretide impact on damaged cardiolipin

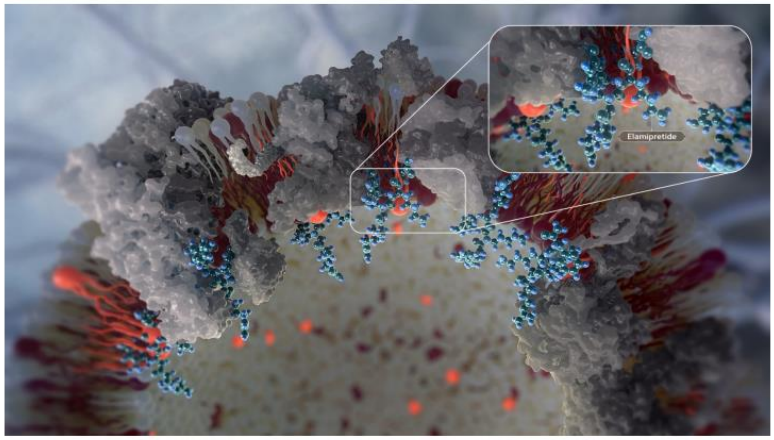


Source: www.stealthbt.com--February 3, 2022

Elamipretide is being evaluated by Stealth for use in diseases involving ophthalmic and rare cardiomyopathies, where there is a genetic basis for the underlying dysfunction and where they have the potential to be expedited. The following graphic gives a deeper dive into how elamipretide modulates inner mitochondrial membrane dynamics that are disrupted:

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





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]

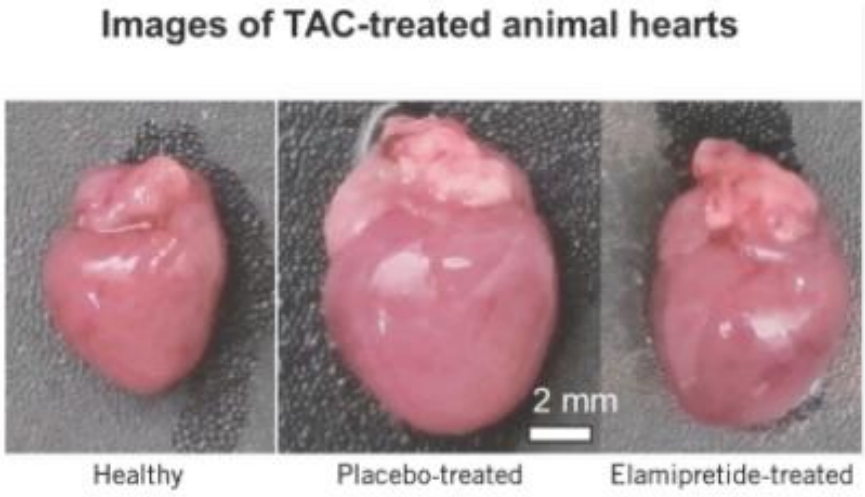
IMM = inner mitochondrial membrane; CL = cardiolipin

[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

Source: www.stealthbt.com--February 3, 2022

As noted above, the company notes that elamipretide has been reported to be well tolerated in clinical trials of over 1,000 subjects systemically exposed to this point, which we believe should help smooth the process of getting approval for trials involving elamipretide and various other genetic conditions. Additionally, Stealth reports that in preclinical and clinical studies researchers have observed that elamipretide increases mitochondrial respiration, improves electron transport function and ATP (adenosine triphosphate) production and reduces formation of pathogenic ROS (reactive oxygen species) levels.

One of Stealth's major focuses is cardiomyopathy-related conditions. Bolstering the prospects for that line of thinking, in our view, was a study of a mouse model of hypertrophic cardiomyopathy published in *Circulation: Heart Failure* in September 2013. In the study, treatment with elamipretide attenuated heart failure induced by transverse aortic constriction, or TAC. As shown in the images below of a healthy mouse heart, a mouse heart with TAC-induced hypertrophic cardiomyopathy treated with placebo, and a mouse heart with TAC-induced hypertrophic cardiomyopathy treated with elamipretide, elamipretide-treated mice retained normal cardiac structure despite the TAC intervention.



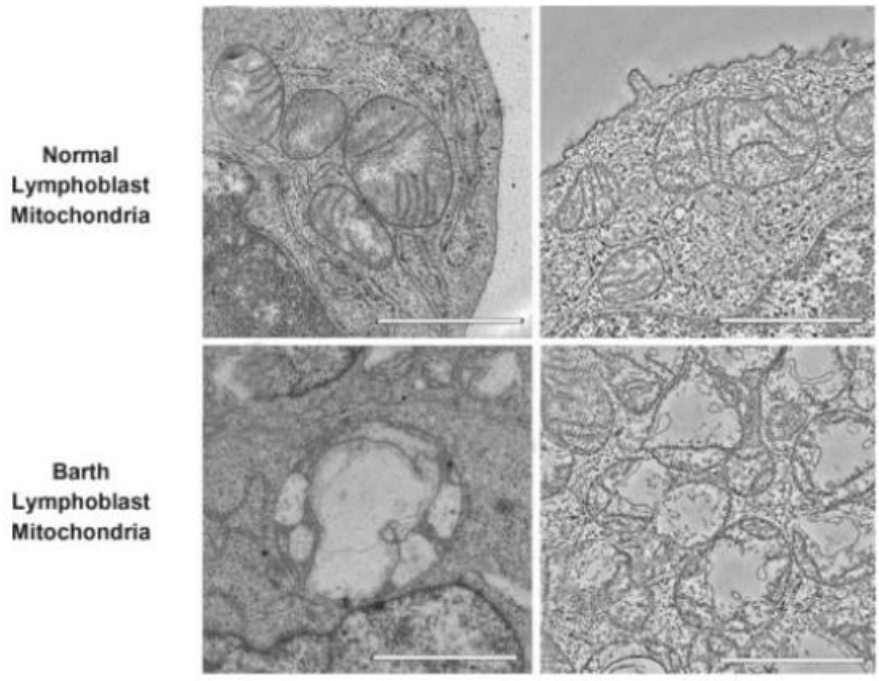
Source: www.stealthbt.com--February 3, 2022

Positive indications such has this has allowed Stealth to pursue treatment for a condition known as Barth Syndrome, where sufferers are searching for a treatment and where none currently exists.

Barth Syndrome

According to the National Institute of Health, Barth syndrome is a rare, genetic disorder of lipid metabolism that primarily affects males. Barth is caused by a mutation in the tafazzin gene, or TAZ, which leads to decreased production of an enzyme required to produce cardiolipin. As we noted above, cardiolipin is an essential lipid that is important in energy metabolism.
Those afflicted with Barth syndrome can expect the following characteristics, which may occur in combination:

- Varying degrees of heart muscle weakness (cardiomyopathy).
- Low white blood cell count (neutropenia), which may lead to an increased risk of bacterial infections.
- Reduced muscle tone (hypotonia)
- Muscle weakness
- Undeveloped skeletal muscles
- Delayed growth
- Fatigue
- Vary degrees of physical disability
- Methylglutaconic aciduria, which is an increase in an organic acid that results in abnormal mitochondrial function. The following picture of lymphoblast mitochondria indicate that, compared to normal mitochondria the mitochondria of people with Barth syndrome have unhealthy morphology. This includes a lack of inner membranes, poor alignment of cristae, and swollen or collapsed segments of cristae.



Source: www.stealthbt.com--February 3, 2022

Barth syndrome, per the Barth Syndrome Foundation, is estimated to impact between 1 in 300,000-400,000 births and there are currently fewer than 300 diagnosed worldwide. Barth syndrome is an X-linked genetic condition that is passed from mother to son through the X chromosome. A mother who is a carrier of Barth typically shows no sign or symptoms of the disorder herself. On average, 50% of

children born to a mother carrying Barth will inherit the defective gene, but only the male children will develop symptoms. On the flipside, all daughters born to an affected male will be carriers of Barth but typically will have no symptoms.

Due the small population of sufferers of Barth syndrome and the potential of elamipretide to treat the condition, Stealth was awarded Fast Track and Orphan Drug designation for that treatment. According to the FDA receiving the Fast Track status makes the treatment or drug eligible for:

- More frequent meetings with the FDA to discuss the development plan and ensure collection of appropriate data needed for approval.
- More frequent written communication from the FDA about the design of clinical trials and use of biomarkers.
- Eligibility for Accelerated Approval and Priority Review
- Rolling Review, which means the company can submit completed sections of its application for review, rather than waiting until every section of the application has been completed. Normally, the FDA will not review the application until all sections have been completed.

Similarly, orphan drug designation qualifies the company for incentives such as tax credits for qualified clinical trials, exemption from user fees and the potential for seven years of market exclusivity after approval.

Stealth has brought elamipretide through completion of phase 3 trials and submitted the NDA (new drug application) for the treatment of Barth but on October 18, 2021, Stealth received a Refusal to File letter from the FDA regarding the NDA for elamipretide for the treatment of Barth syndrome. The FDA determined, upon its preliminary review, that the NDA was not sufficiently complete to permit a substantive review. In the letter, the FDA stated that the NDA does not contain an adequate and well-controlled trial that provides evidence of effectiveness, noting that the SPIBA-201 Phase 2 clinical trial of elamipretide for the treatment of Barth syndrome was negative during the randomized, double-blind portion of the study and that the FDA does not consider the open label extension of the SPIBA-201 trial to be adequate and well-controlled.

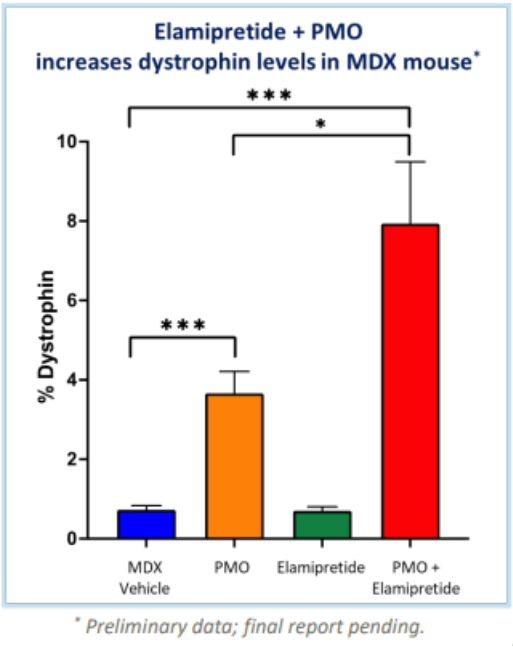
This recent development is concerning to us, especially given the lack of treatments using mitochondria-directed methods approved to this point, but we are holding back judgement until Stealth meets with the FDA. A Type A meeting is necessary for proceeding with a stalled product development program or addressing an important safety related issue and Stealth has completed that meeting and called it “constructive”, with plans for more discussion with the agency in an attempt to move toward approval. We anticipate that we will have further opinion on this treatment’s potential for potential revenue generation as those discussions evolve and note that the Barth community is supportive of elamipretide, with over 4200 supporters signing a petition of support that was sent to the FDA along with more than 730 testimonials according to the Barth Syndrome Foundation. We also note that the most valuable aspect of the Barth trials may end up being the learning that occurred during the process that can be applied to other treatments.

Duchenne muscular dystrophy and Friedrich’s Ataxia

Another condition that Stealth believes elamipretide has the potential to treat is Duchenne muscular dystrophy (DMD). DMD is a rare genetic disease that causes the muscles in the body to become weak and damaged over time, eventually becoming a fatal condition. At the current time, there are no known treatments available, DMD is irreversible and is diagnosed in patients at an average age of 5 and progresses rapidly to the point that 90% of sufferers are in wheelchairs by age 15. Again, this is a disease that primarily affects males, with about 1 in 3,500 males being born with DMD.
DMD is caused by a genetic mutation that prevents the body from producing dystrophin, which is a protein that muscles need to work properly. Without dystrophin, muscle cells become damaged and weaken. Stealth is reporting that elamipretide has shown some initial success at treating the heart

muscle in DMD patients. The heart is obviously a vital muscle for everyone and DMD sufferers often end up losing their battle with the disease due to heart failure, with the average age of death for patients with cardiomyopathy being 19.6 according to research compiled by Stealth. The company noted that data showed improvement in mitochondrial respiration and heart muscle function in explanted tissue from a dystrophic heart (heart condition of a child with Becker muscular dystrophy). Researchers also note that the study showed that elamipretide treatment improved mitochondrial respiration, contraction and relaxation in muscle fibers isolated from failing hearts of children with dilated cardiomyopathy. As a result of these potential positive developments, Stealth has scheduled a pre-IND meeting, which is typically a first meeting with the FDA to discuss the process of getting a treatment through trials, with the Division of Cardiology and Nephrology (DCN) within the FDA to discuss a potential development plan for elamipretide and DMD and we'll be watching for updates for the results of that meeting.

A very recent preclinical study showed that elamipretide could had other positive effect on DMD sufferers. Studies involving mice showed that adding elamipretide to the existing PMO (phosphorodiamidate morpholino oligomer) treatment more than doubled the increase in dystrophin levels versus the PMO treatment alone:



Source: www.stealthbt.com--February 9, 2022

As a result of the increase in dystrophin levels, Stealth researchers saw a decrease in fibrosis and inflammation, a blunting of the loss of muscle mass and increase of regeneration, correcting aberrant cellular calcium handling and correcting blood flow regulation.

These are very early results, but potentially important to the company as it may lead to another path for approval of elamipretide for DMD sufferers.

The final condition, for now, with a heart-related element to it that Stealth is investigating elamipretide for treatment of is Friedrich's ataxia, which is the most common form of ataxia, affecting about 1 in 40,000 people in the United States. Friedrich's ataxia is an inherited, genetic disease that damages the spinal cord, peripheral nerves and the cerebellum portion of the brain. The condition typically develops in children and gradually grows worse over time. Friedrich's is caused by a genetic defect in the gene labeled FXN, which carries the genetic code for a protein called frataxin. In preclinical studies, elamipretide has been shown to improved mitochondrial structure and function as well as increasing mature frataxin levels in Friedrich's patient lymphoblasts. As a result of these positive developments, the researcher involved in this study has submitted a Phase 2a clinical trial to the FDA and is currently waiting for Institutional Review Board approval. Stealth is supporting the

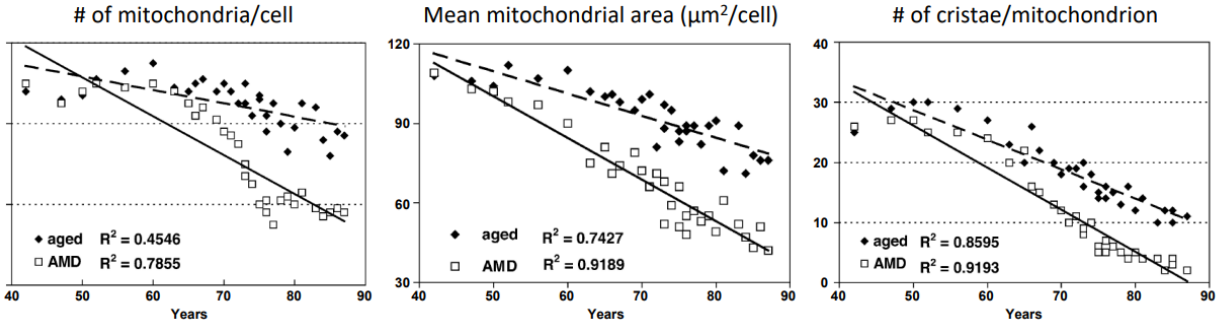
study in the assessment of the impact of elamipretide in a cohort of patients affected by cardiomyopathy and/or visual decline associated with Friedrich's.

Ophthalmic Diseases

Stealth Biotherapeutics notes that normal mitochondrial play a critical role for ocular function and dysfunctional mitochondria play a part in several rare and common diseases of the eye. The company also notes that ophthalmologic diseases that have not traditionally been considered to have obvious mitochondrial origins are increasingly recognized to result at least in part from impaired mitochondrial function. Oxidative damage that results over time from inherited mtDNA mutations or prolonged oxidative stress instability leads to cumulative mitochondrial damage, which is recognized to be an important factor in disorders such as dry age-related macular degeneration (AMD) and Leber's hereditary optic neuropathy (LHON).

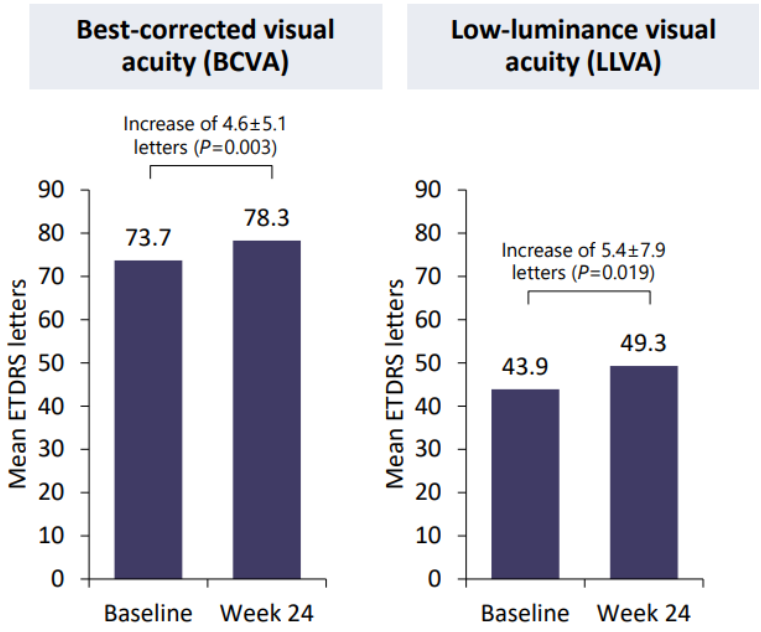
Stealth is pursuing elamipretide for treatment of geographic atrophy (GA), which is an advanced form of AMD. AMD is estimated to impact more than 10 million people in the United States and there are no known treatments for the disease. AMD results in distorted vision—more specifically, a reduction in low luminance visual acuity, reduced overall visual acuity and blurred vision—and is the leading cause of blindness among older adults in the developed world.

According to the National Institute of Health (NIH), recent evidence suggests that mitochondrial damage and oxidative stress in the retinal pigment epithelium (RPE) may play an important role in AMD. As seem in the graphic below, RPE mitochondria in AMD eyes undergo more pronounced degenerative changes, with lower mitochondrial density, organelle area and cristae number.



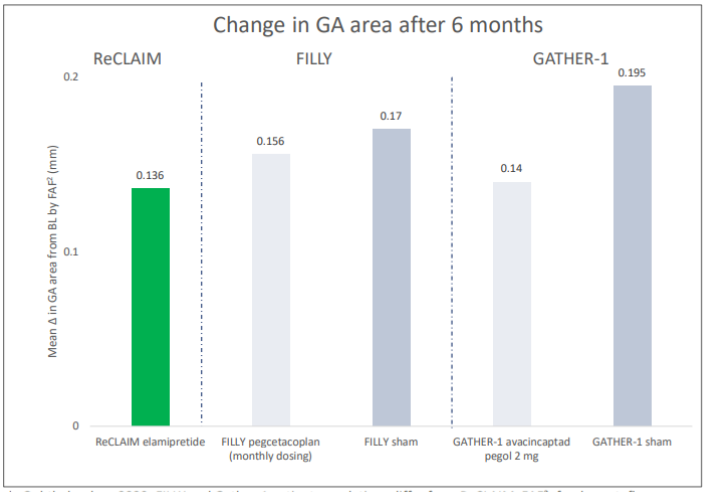
Source: www.stealthbt.com--February 3, 2022

The results of the Phase I trial, known as the ReCLAIM Study, are in the table below. It's important to know that the ETDRS letter test is the standard eye test that almost everyone has probably seen with the bigger letters at the top that get gradually smaller as you move down the chart. Also, researchers believe that low luminance visual acuity may be a better test to identify AMD at an earlier stage—so both test results are presented below:



Source: www.stealthbt.com--February 3, 2022

Other Phase I results from a different patient group show that the area impacted by GA is less in patients treated with elamipretide.



[1]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

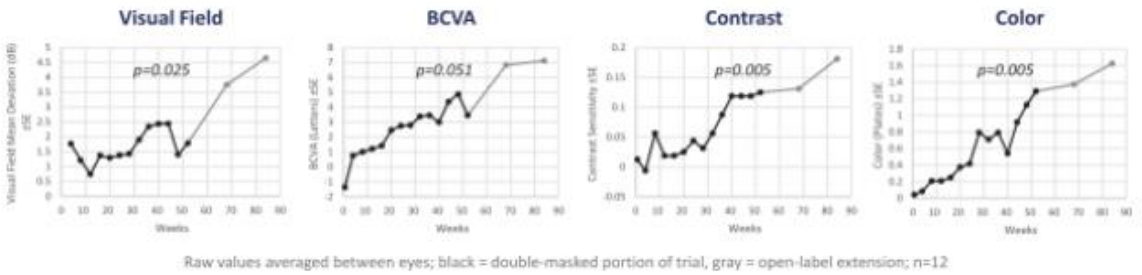
Source: www.stealthbt.com--February 3, 2022

As a result of the Phase I portion of the ReCLAIM trial, the Phase 2—known as ReCLAIM 2—trial was just completed and the results are expected in the first half of 2022.

Stealth is also investigating elamipretide for the treatment of Leber's hereditary optic neuropathy (LHON), which is mitochondrial disease that affects the eyes and is characterized by central vision loss. The initial clinical expression of LHON is often a sudden and painless central vision loss, frequently accompanied by loss of color vision and reduced visual acuity. Stealth estimates approximately 10,000 people in the United States have LHON. There are no approved treatments in the US for LHON, although a treatment known as Raxone has been approved in Europe for the treatment of LHON.

Stealth believed that, based on preclinical and early clinical findings, systemic elamipretide may be beneficial for subjects with LHON. In preclinical trials, elamipretide was observed to improved

mitochondrial function under oxidative stress in mouse-derived retinal ganglion cells, which are the cells most affected by LHON. Experiments in a mouse model of acute traumatic optic neuropathy also suggest that systemic administration of elamipretide post-trauma may improve retinal ganglion survival and visual function, supporting the plausibility of therapeutic benefit in the presence of LHON-associated, oxidative-stress mediated damage of the optic nerve. The results from the Phase 2 trial, known as ReSIGHT 2, as well as a 6-month open label extension are presented below:



Raw values averaged between eyes; black = double-masked portion of trial, gray = open-label extension; n=12

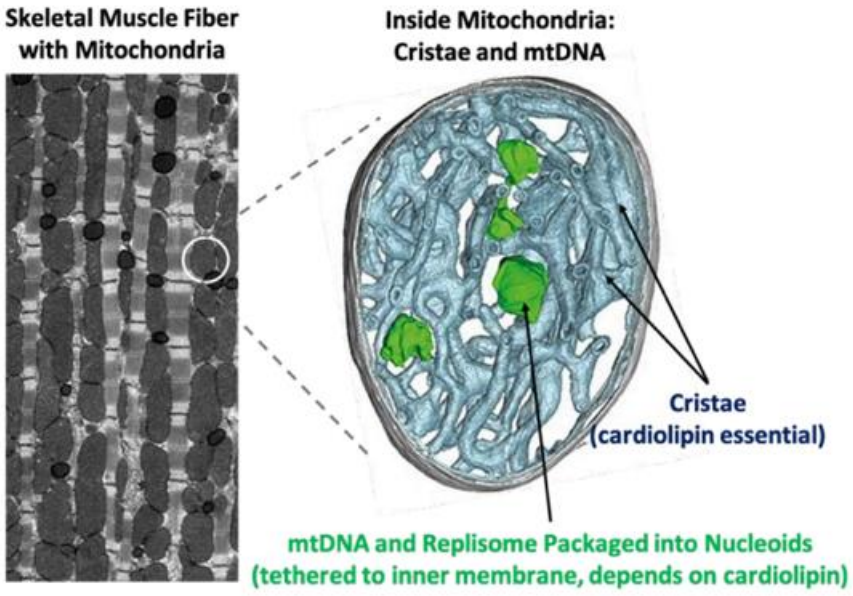
Source: www.stealthbt.com--February 3, 2022

As a result of these positive results, the FDA approved the pivotal Phase 3 clinical trial and Stealth is currently investigating the appropriate formulation of elamipretide to use for the trial and is forecasting a final decision on that early this year, after which Phase 3 would begin.

Neurological Diseases

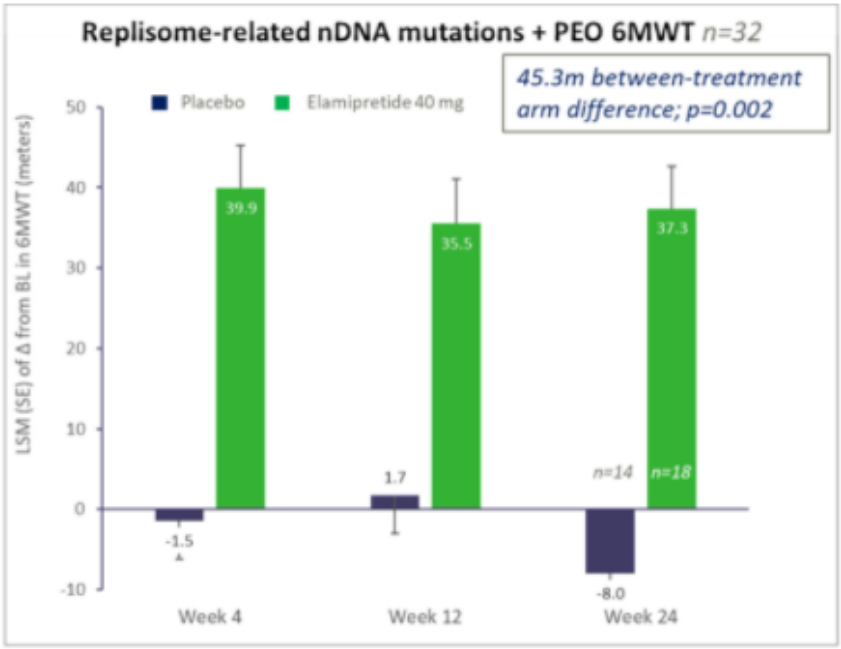
There are a group of disorders associated with changes in genetic material found within the DNA of mitochondria (mtDNA) known as primary mitochondrial myopathies and genetic disorders in genes outside the mitochondria (nuclear DNA or nDNA) that Stealth is investigating the use of elamipretide for. Specifically, Stealth is enrolling patients for a Phase 3 trial for elamipretide treating nuclear primary mitochondrial myopathies (nPMM) which are genetically defined disorders leading to defects of oxidative phosphorylation, affecting predominantly, but not exclusively, skeletal muscle. Stealth has received Fast Track and Orphan Drug designations from the FDA for the development of elamipretide for this purpose.

Results from a previous study that was more broadly targeted and involved elamipretide treating primary mitochondrial disease, which is a disease characterized by debilitating skeletal muscle weakness, exercise intolerance and fatigue, led them to focus in on nPMM. During the study, a subgroup of patients with nuclear genetic mutations, most of whom had mutations in nuclear genes encoding for protein necessary for mtDNA replication, also known as replisome-related mutations. Researchers theorized that this may be due to cardiolipin, which is the target for elamipretide, is involved in mitochondrial protein and metabolite transporters and machinery associated with mtDNA packaging and replication. Researchers then did a post hoc analysis on the subjects with replisome-related nDNA mutation in combination with a diagnosis of progressive external ophthalmoplegia (PEO), which is the progressive weakening of the eye muscles thought to almost always be observed with skeletal muscle involvement in this disease.



Source: www.stealthbt.com--February 3, 2022

This post hoc analysis produced some encouraging results in the 6-minute walk test (6MWT), which is a standard test of physical condition, shown below:



Source: www.stealthbt.com--February 3, 2022

These positive results, which showed a 45+meter difference between the patients receiving elamepretide versus the placebo, have led to the study that is currently being undertaken and enrolling patients for a Phase 3 trial.

SBT-272

Elamipretide is not the only compound that Stealth is developing. In fact, although it's early in the process, early indications from the compound known as SBT-272, in our view, may end up being the most consequential development from Stealth out of the current potential treatments—both in terms

of impact on patients and the commercialization possibilities. Stealth's primary objective in designing SBT-272 was to increase brain exposure compared to elemipretide due to the potential that mitochondrial may be beneficial in neurological disorders such as amyotrophic lateral sclerosis (ALS), Parkinson's, Huntington's and Alzheimer's.

Preclinical data, according to Stealth, showed that SBT-272 demonstrated a three times greater concentration of the compound in the brains of rats compared to elamipretide and 25 times greater area under the concentration-time curve—both of which suggest that SBT-272 has both higher brain exposure and greater residence time. Following is a table showing areas in preclinical studies where SBT-272 has shown indications of improving the condition—we don't want to project forward too much given these indications, but it does provide some clues as to what may be coming in the future and give both Stealth and the FDA some pathway to designing the approval process:

	Cerebral ischemia reperfusion	ALS (SOD-1)	ALS (TDP-43)	Huntington's*	Alpha-synucleinopathy	Frontotemporal dementia (FTD)
Also relevant for:	*stroke*		*FTD*		*Parkinson's; multiple system atrophy; Lewy Body Dementia*	*Supranuclear palsy (PSP) Primary tauopathy*
Mito-protection	✓		✓	✓	✓	✓
Neuroprotection			✓		✓	✓
Brain metabolism				✓		
Reduction of protein aggregates					✓	✓
Motor deficit		✓		✓		
Anti-inflammatory					✓	

Source: www.stealthbt.com--February 3, 2022

Stealth is at the beginning stages of moving SBT-272 through the approval process with the Phase I trial forecasted by the company to begin in the first half of 2022 and we will be watching the developments of this compound carefully.

Delivery

An often overlooked, in our experience, part of the treatment process is the delivery of the compound to the appropriate locations within the body to have an impact. This is something that Stealth's management notes it has extensive experience in optimizing delivery of compounds to mitochondria, which has been a challenge for other drug delivery technologies. Stealth has demonstrated capability to deliver beneficial payloads to mitochondria by conjugating them with their proprietary compounds, which serve as vectors or carriers to mitochondria. This approach has the potential to confer mitochondrial specificity to promising therapies that do not otherwise localize to mitochondria, potentially increasing the efficacy of a payload by targeting it to the part of the cell where it is needed most.

These "payloads" might include small molecules, proteins, oligonucleotides, nanoparticles and liposomes and Stealth's "carrier program" (what the company calls their delivery strategy) has the potential to create new pipeline assets from known delivery of small molecules, enzymes, proteins or therapeutic genes to address inherited mitochondrial disorders.

THE INVESTMENT STORY

Stealth Biotherapeutics is a clinical-stage biopharmaceutical company focused on the discovery, development, and commercialization of novel therapies for diseases involving mitochondrial dysfunction. Mitochondrial research is still in its, relatively speaking, early stages and we have seen multiple misfires or stalled development programs across the biotechnology universe, leading to what we perceive to be investor skepticism regarding the commercialization of related therapies. We understand that sentiment, as the reality of mitochondrial research hasn't seemed to match the early hope held by patients and investors alike, at least not yet. However, we would caution against becoming overly skeptical and realize there have been some successes and with each "failure", learning occurs and the proverbial mitochondrial ball is pushed closer to the end zone.

In our view, several key issues lead us to believe that Stealth may ultimately cross that line and be able to bring new therapies to the market. The first thing to remember is that, despite the disappointments in some cases, mitochondrial treatment research is creating exciting possibilities. Stealth, for example, as detailed above, is currently pursing treatments for such diseases as dry AMD, which causes blindness for millions, heart conditions of varying names that are impacting thousands of lives and conditions plaguing many in the United States and around the world such as Alzheimer's and dementia. And while the treatments that we've discussed above aren't across the finish line yet, they have clinical results that show at least some level of success while proving to be safe for patients to use, allowing the approval processes to move forward.

The number one issue we see is one that impacts many companies at this stage of life—can Stealth obtain the funding it needs to continue its research and testing needed to shepherd these therapies to approval and commercialization? At this point, Stealth management reports that they have the funding needed for continue operation through the third quarter of 2022. Certainly, we would like to see a greater level of funding on hand to give us a little more comfort in Stealth's ability to continue, but we feel fairly confident that, at least for the foreseeable future, Stealth will obtain the capital they need to continue. As of August 2021, Stealth reported that Morningside Venture Investment Limited owned 72.5% of the company, representing a large commitment by the firm to Stealth—one that we do not believe Morningside, or any investment firm, would like to see disappear, leading us to believe that further financial support would be forthcoming should it be required-at least in the near term. Also, Stealth entered in a development funding agreement with Morningside in October 2020, which states that Morningside will provide funding to Stealth to support "efforts to secure regulatory approval for elamipretide and to develop elamipretide for the treatment of Barth, dry AMD, FRDA, Duchenne cardiomyopathy, nPMD and LHON.

We are also of the opinion that larger biopharma and drug companies will be interested in partnering with, investing in, or acquiring Stealth due to the advances they have made in the mitochondrial research and the delivery system they have developed. Additionally, it is that delivery system, discussed above, that may be the first "product" that Stealth is able to market and begin to bring in revenue to the company.

The therapy that we currently believe has the most potential to come to market and garner substantial interest from patients is the dry AMD therapy involving elamipretide. Discussed in more detail above, the dry AMD market is a large one with more than 10 million people being impacted in

the United States. There are no current treatments for dry AMD and it is the leading cause of blindness for older adults in the developed world, leading us to believe that there would be a solid demand for a treatment that could improve and extend the sufferers eyesight. As such, we will be anxiously awaiting the results of the current Phase 2 trial that was recently completed.

With regard to Barth syndrome, we are cautiously optimistic regarding the potential of FDA approval of the elamipretide treatment, although, here too, we are eager to see the results of the meeting with the FDA scheduled for the first quarter of 2022 regarding what's necessary to gain approval. Judging by what we've seen in other cases, we also believe that there is the possibility that Stealth is granted a Rare Pediatric Disease Priority Review Voucher from the FDA. Barth certainly has the seriousness required and Stealth has already received Orphan Drug and Fast Track status for elamipretide in the treatment of Barth syndrome. Once received, Stealth could either use or sell the voucher. Recent voucher sales have been in the $90-100 million dollar range. Although such a designation is certainly not assured, we believe the possibility of receiving one should be in the investment calculus when considering Stealth.

Finally, an investment in Stealth ultimately, in our view, comes down to the belief in the leadership of the company and the processes and vision they have that plays a big part in whether MITO is a stock worthy of consideration. And it is in the talking with management and diving into their research process that makes us believe that Stealth is worth a look for investors that have a higher risk tolerance. Of course, there are risks, some of which are outlined below, but we believe there is upside potential as well. Stealth research is focused on a specific segment of the mitochondria—cardiolipin—which plays a vital role in many human functions, rather than the broader whole mitochondria itself, which we believe leads to a better possibility of success. From discussions with management and digesting statements and presentations they have given in the past, we came away impressed with the dedication and knowledge of the science displayed and believe that the team in place is a solid one to take Stealth to the next level.

VALUATION

As with any investment, the attractiveness of a possible stock purchase is largely based on what the current price of the stock is versus what the investor calculated the appropriate, or fair, value to be. With a company such as Stealth, opinions regarding the appropriate valuation can vary widely, due to the uncertainty of future cash flows. For example, Stealth's Barth treatment made it through Phase 3 trials, only to be stopped by the FDA, resulting in the upcoming meeting with the management of Stealth to discuss what must occur to garner approval. Any future revenues from that treatment are extremely uncertain at this point, making valuation a bit more difficult and leading to the possibility of a wide range of outcomes.

Most often we move to the more conservative side of the ledger when approaching valuation, giving investors, in our view, a solid valuation estimate with the possibility of an implied upside call option if certain projects turn out to be better than expected.

With Stealth, ticker symbol MITO, which is traded as an ADS on the NASDAQ, our view is that the stock is currently undervalued. Rarely can we be sure why a company is undervalued compared to what we believe the analysis shows it should be valued at, but we believe that investors are reflecting the skepticism regarding mitochondrial treatments we believe is building, while not give Stealth the credit for the advancement in focused mitochondrial research the company has made, their diverse pipeline, or the possibility of a partnership or acquisition by a larger medical company.

We believe, taking what we view as a very conservative view of the future cash flows of Stealth, that a fair value for Stealth is $2.10.

We arrive at that valuation by assuming that Stealth has one treatment reach commercialization status within the valuation horizon timeline—that of dry AMD, which we believe has the most potential for approval combined with the market that we believe is the most attractive at the present time. We assign a 20% probability on the approval of elamipretide for the treatment of dry AMD by 2025 with commercialized selling beginning in 2026. We admit that number is a bit arbitrary, but it is also based on historical drug approval evidence. According to the American Council on Science and Health, which cited a study from MIT that looked at drug and vaccine candidates for approval and how many of them eventually received approval. According to the study, 20.9% of submitted non-oncology therapies are successful in obtaining FDA approval. The percentage is somewhat higher for those candidates that reach Phase 2, which elamipretide has for the treatment of dry AMD, but given the lack of success that mitochondrial treatments have had in receiving approval that we've seen, we believe keeping the probability at 20% is appropriate.

We then estimate that Stealth will be able to capture 1% of the estimated 10 million person dry AMD market in 2026 and is able to grow that by 10% the first year and 5% in the following years. On the cost of goods sold side, we are estimating an 80% gross margin for Stealth, which is roughly in line with other therapies we've seen from biotech companies we've covered, if not a little low.

Other expenses are grown at 5%, but we add in a major new expense in 2026 for marketing. We believe that the marketing budget for an approved elamipretide is going to have to be extensive due to the uniqueness and newness of the mitochondrial treatment. We assign the marketing cost to be 20% of the overall sales revenue through the valuation timeline.

We readily admit that there is certainly the possibility that other treatments, perhaps some we've not even mentioned, may come to fruition, including that of Barth Syndrome, which has already completed Phase 3 trials. At this point, however, we view those possibilities at too small to be statistically significant and view them as a sort of upside call potential on an investment in MITO.

RISKS

- One of the primary risks to Stealth that we see is the need for additional funding. Should they not be able to obtain the needed funding, Stealth being able to continue as a going concern could be in question.
- Stealth has no history of commercializing a therapy, which could lead to missteps, oversights and mistakes with regard to marketing, relationships with various parties and other potentially important issues.
- Mitochondrial research in general has not proven to be very successful at garnering FDA approvals and bringing therapies to market.
- Being able to retain key employees could be difficult and cause problems if the company is unable to do so.
- There are other companies pursing therapies along a similar way of thinking and should they have similar therapies come to market prior to Stealth's being able to be marketed, demand for the Stealth therapy would likely be diminished.
- The possibility that Stealth has none of their therapies approved by the FDA exists.

- Stealth relies on third parties for manufacturing and distribution, and should those relationships change in a substantially negative way, Stealth may have difficulty continuing their march toward commercialization.

MANAGEMENT

- Reenie McCarthy is the Chief Executive Officer and a member of the Board of Stealth BioTherapeutics. Reenie is a 20+ year veteran of the investment team of Morningside, Stealth's principal investor, with extensive experience working with private nonclinical and clinical stage companies developing drugs across a broad spectrum of therapeutic areas.

- Brian Blakey is the Chief Business Officer of Stealth BioTherapeutics. He has 30 years of pharmaceutical marketing, alliance development and operations experience prior to Stealth. Previously, Brian was the COO of Element Marketing Group and the Vice President of Commercial Development at Salutria (formerly AtheroGenics). He has held senior positions at other pharmaceutical companies, including GlaxoSmithKline. Brian holds a Doctor of Pharmacy degree from the University of Florida.

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

- Marty Redmon is Chief Research & Development Officer at Stealth BioTherapeutics. Marty has more than 25 years of experience in pharmaceutical R&D, operations, and project and functional line management. Prior to joining Stealth, he served as Senior Vice President of Research, Development and Technical Operations at Precision Dermatology, and has previously held pharmaceutical development positions at Eli Lilly, Focal, Sepracor, Praecis, and ArQule. He has experience managing R&D and manufacturing organizations responsible for development of a broad range of therapeutics in a variety of dosage forms. Marty holds a BS in Chemical Engineering and a PhD in Pharmaceutical Sciences, both from the University of Kentucky.

- Rekha Sathyanarayana is Vice President, Clinical Operations at Stealth BioTherapeutics. Rekha has more than 23 years of diverse therapeutic experience in pharmaceutical development, of which 12+ years have been serving in a key leadership position as Head of Clinical Operations, responsible for strategic oversight, budget and functional line management. Rekha has overseen global pivotal trials at Pharma, CRO and Biotech that culminated in bringing 6 commercial products to market. Prior to joining Stealth BioTherapeutics, Rekha was Vice President Clinical Operations at Titan Pharmaceuticals leading programs in Parkinson's Disease and Opioid addition, including receiving a NIDA grant. Previously, she led her department through IND and BLA enabling programs at Revance Therapeutics. At Bavarian Nordic A/S, she led cancer vaccine program. At Depomed Inc, she was pivotal in securing NDA approvals of 3 commercial products. She also had increasing responsibilities at Neopath Inc, R2 Technologies, PPD Inc and Abbott Labs that yielded 510K & NDA approvals. Rekha holds a BS in Microbiology from Bangalore University and an advanced BS in Medical Technology from Northern Illinois University.

PROJECTED INCOME STATEMENT & BALANCE SHEET

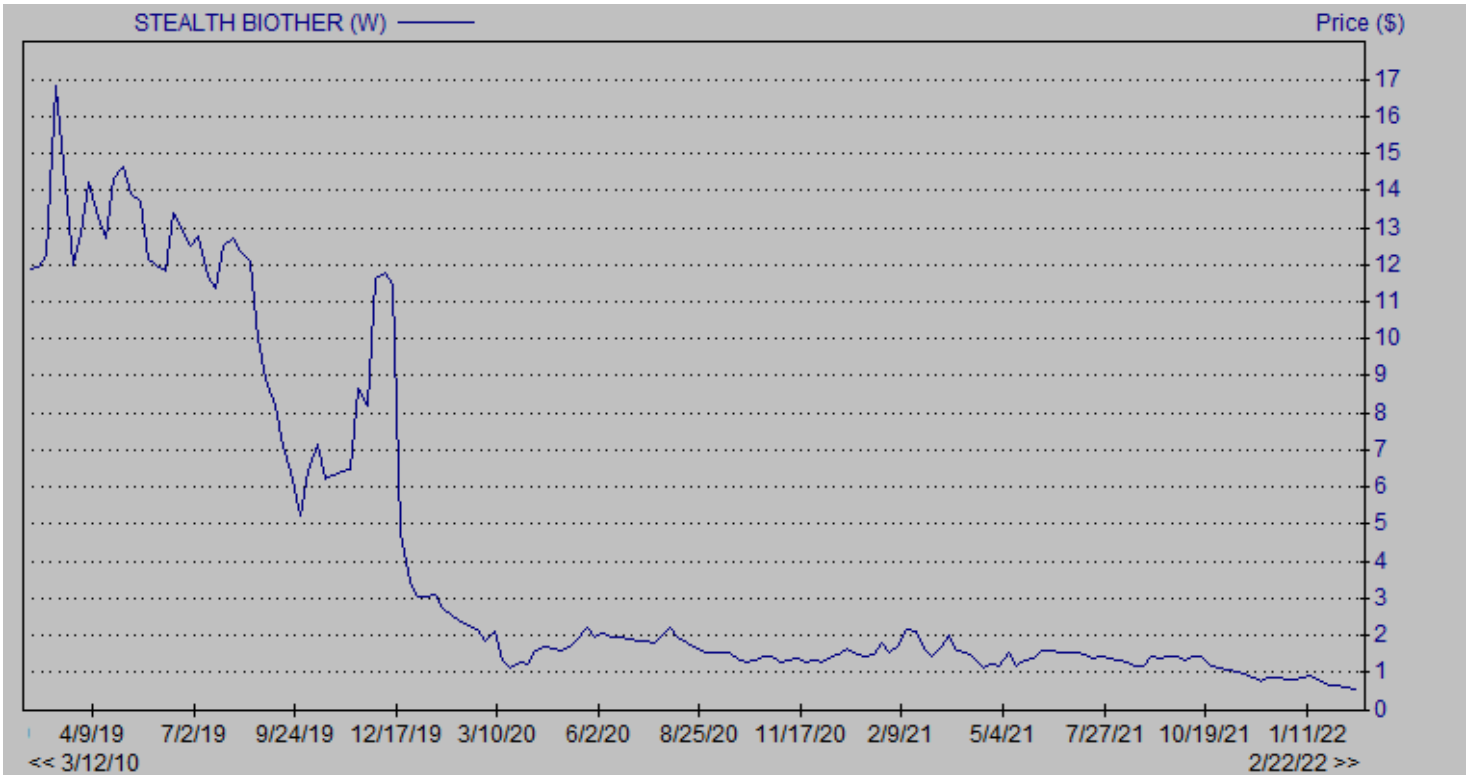
Steath BioTherapeutics Income Statement
(in thousands, except per share data)

	1Q2021A	2Q2021A	3Q2021A	4Q2021E	2022E	2023E	2024E
Revenues							
Grant Revenue	0	0	0	0	0	0	0
Other Revenue	0	0	0	0	0	0	0
Total Revenues	0	0	0	0	0	0	0
Cost of Revenue	0	0	0	0	0	0	0
Gross Profit	0	0	0	0	0	0	0
Operating Expenses							
Research and Dev.	6,099	5,913	6,739	6,806	27,226	27,498	27,773
General Admin.	4,979	5,083	4,707	4,754	19,206	19,399	19,592
Total Operating Expenses	(11,078)	(10,996)	(11,446)	(11,560)	(46,432)	(46,896)	(47,365)
Gain/(loss) from operations	(11,078)	(10,996)	(11,446)	(11,560)	(46,432)	(46,896)	(47,365)
Other income and (expenses)							
Interest expense	(300)	(188)	(196)	(200)	(880)	(968)	(1,065)
Other	3,689	(7,222)	5,345	0	0	0	0
Total other income/(expenses)	3,389	(7,410)	5,149	(200)	(880)	(968)	(1,065)
Net Gain/(loss)	(7,689)	(18,406)	(6,297)	(11,760)	(47,312)	(47,864)	(48,430)
Net gain/(loss) per shareholder	$ (0.01)	$ (0.03)	$ (0.01)	$ (0.02)	$ (0.07)	$ (0.06)	$ (0.06)
Basis and diluted wtd avg common shares	652,807,323	674,737,590	692,513,064	699,438,195	720,421,340	742,033,981	764,295,000

Stealth BioTherapeutics Balance Sheet
(in thousands, except per share data)

	1Q2021A	2Q2021A	3Q2021A	4Q2021E	2022E	2023E	2024E
Assets							
Current Assets:							
Cash and equivalents	32,060	30,766	42,277	44,391	46,610	48,941	51,388
Other current assets	1,927	844	1,163	1,228	1,297	1,370	1,446
Total Current Assets	33,987	31,610	43,440	45,619	47,907	50,310	52,834
Property and equipment	92	72	115	127	139	153	168
Other non-current assets	702	576	632	638	645	651	658
Total Assets	34,781	32,258	44,187	46,384	48,691	51,115	53,660
Liabilities and Shareholder Equity							
Current liabilities:							
Accounts payable	4,620	2,566	3,915	3,993	4,073	4,155	4,238
Other current liabilities	4,350	5,397	5,743	5,858	5,975	6,095	6,216
Current portion of debt	7,236	5,452	0	0	0	0	0
Total current liabilities	16,206	13,415	9,658	9,851	10,048	10,249	10,454
Development derivative liability	30,643	45,152	49,817	49,817	54,817	59,817	64,817
Long-term portion of debt and other	11	6	13,544	13,544	18,542	23,542	23,542
Total Liabilities	46,860	58,573	73,019	73,212	83,407	93,608	98,813
Total Shareholders Deficit	(12,079)	(26,315)	(28,832)	(26,828)	(34,716)	(42,493)	(45,153)
Total Liabilities and Shareholder Equity	34,781	32,258	44,187	46,384	48,691	51,115	53,660

HISTORICAL STOCK PRICE



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