Targeting the powerhouse of cells to improve the lives of mitochondrial disease patients

October 1, 2023

Corporate Presentation

ABLIVA

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Abliva is focused on becoming a global leader in mitochondrial medicine

Experienced team with 20+ years in mitochondrial research and drug development

- Offices in Lund (Sweden) and Boston (US)

Full **R&D capabilities** with a plan to **build to commercialize lead asset**

Portfolio of first-in-class clinical assets to treat **Primary Mitochondrial Disease (PMD)**

- Pivotal Phase 2 study ongoing for KL1333
- NV354 is ready for Phase 1

Publicly traded on NASDAQ Sweden (ABLI, small cap)

- SEK200M (approx. $20M) raise completed in June 2022

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The Abliva portfolio includes two rare disease, first-in-class programs

- **Lead program, KL1333, commenced pivotal Phase 2 study in late 2022**
  - 12-month adaptive design study; 120-180 adults with mtDNA mutations with systemic disease, fatigue and muscle weakness
    - Interim analysis in 2024 will include 40 patients dosed for 6 mo; evaluate futility and include sample size adjustment
  - Positive efficacy data in placebo-controlled Phase 1b study
  - No safety signals or SAEs across multiple studies (>100 subjects treated)
  - Indication of high unmet need with >$1bn blockbuster peak sales potential
  - Strong patent protection with ODD in US, EU
- **Pipeline asset NV354, preparing for Phase 1, targets pediatric neurological diseases**

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2023 News

- Dag Nesse announced as VP, Clinical Operations, in February
- NV354 patent granted in the U.S. on February 2
- Shareholders endorsed warrant program for team and Board in March and May
- NV354 received Orphan Drug Designation in the U.S. in April
- First patient dosed in KL1333 FALCON study achieved in June
- KL1333 received Fast Track Designation in September

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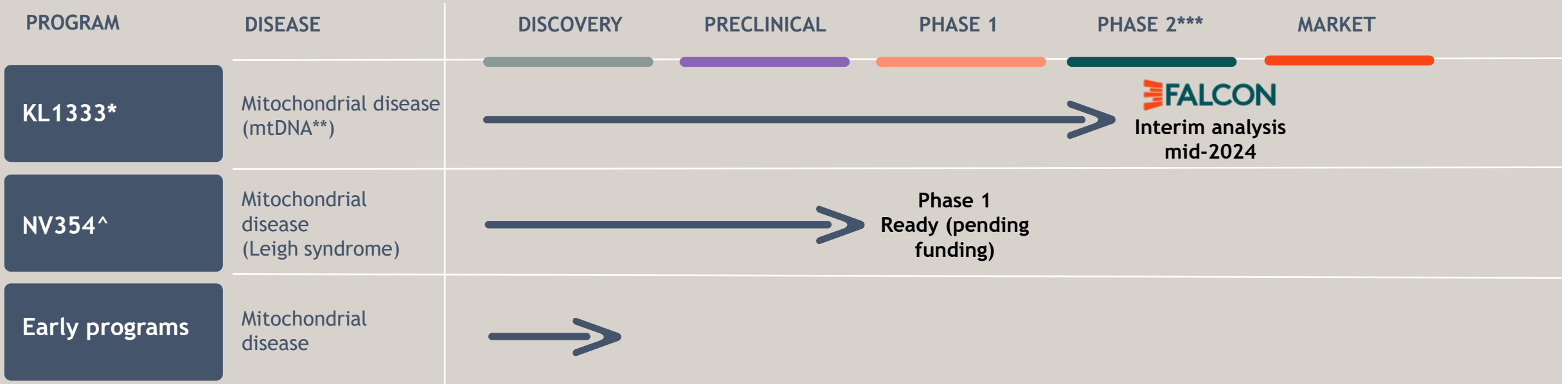
A portfolio of first-in-class therapies targeting underlying pathology in Primary Mitochondrial Disease (PMD)



*Orphan drug designation in the US and Europe. Fast track designation in the US.
^Orphan drug designation in the US
**mtDNA-related mitochondrial disease caused by mutation(s) in mitochondrial DNA (as opposed to nuclear DNA).
***Given that mitochondrial disease is an orphan disease, a Phase 2 study in these patients, if successful, can have the potential for market approval.

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Sparse Competitive Landscape is Defined by Old Mechanisms of Action

Molecule	Company	Mechanism	Notes	
Mavodelpar (REN001)	Reneo Pharmaceuticals	PPARd	Compound originally developed by Novo Nordisk, then by TransTech/vTv. Several disease areas initially being investigated. Readout of PMM trial late 2023.	Muscle focus
Bocidelpar (ASP0367)	Astellas	PPARd	New compound, evaluated in several disease areas, no patient data before phase 2/3 PMM study initiated	Muscle focus
Vatiquinone (PTC743)	PTC Therapeutics	Oxidative stress modulator (15-lipoxygenase)	Numerous trials performed in several disease areas without any clear efficacy signals reported. Current focus on Friedreich's ataxia	Neurology focus
Zagociguat (CY6463)	Tisento Therapeutics (formerly Cyclerion Therapeutics)	Guanylate cyclase (sGC) stimulator (amplifies NO signaling)	Being evaluated in multiple neurological disease areas, Open-label MELAS phase 2a completed	Neurology focus
Sonlicromanol (KH-176)	Khondrion BV	Oxidative stress modulator	Phase 2a study in m.3243A>G patients showed predominantly neutral results across multiple endpoints. Phase 2b study failed primary endpoint, positive changes in post-hoc analyses and open-label extension	Neurology focus

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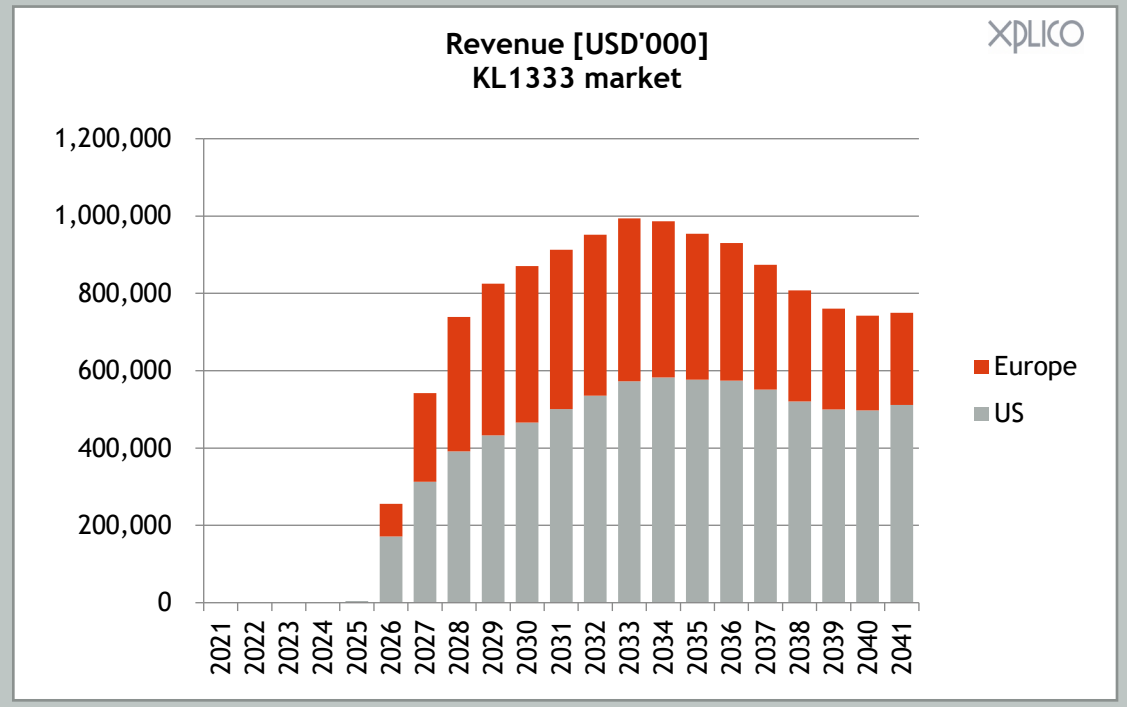
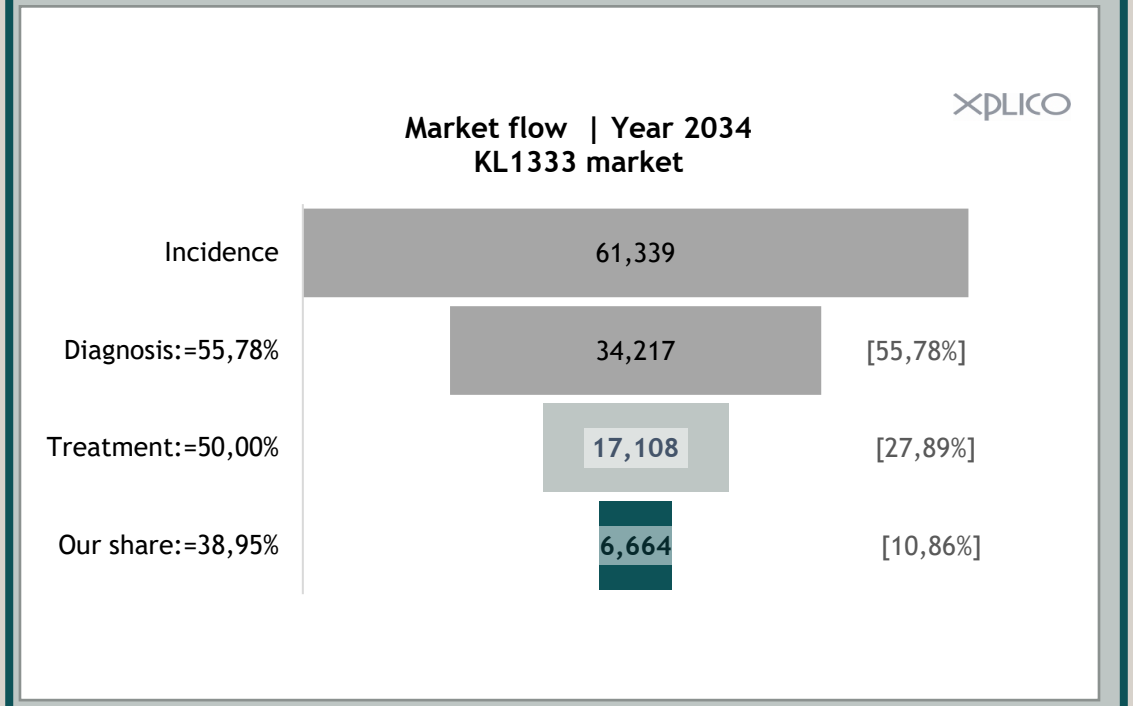
Even with conservative assumptions, KL1333 has blockbuster potential

Base case TPP: Peak sales $1.0B in US, EU



Assumptions: KL1333 treated population on the right; US price of $160K/year (EU $80K)

PMD population & KL1333 market



Investors and pharma recognized the opportunity before Abliva hit the radar

Stage	Year	Deal Type	Companies	Details
Phase 1	2017	Acquistion	Mitobridge acquired by Astellas	$225M upfront; $225M additional dependent upon progress
Phase 2 (Pivotal)	2019	Acquisition	Modis/Zogenix	$250M upfront, $150M milestones, 5% revenue; F-Prime, Orbimed
Phase 2	2019	Acquistion	PTC/BioElectron	$210M (upfront+ milestones)
Preclinical	2020	Acquistion	Nanna Therapeutics/ Astellas	£12M upfront; £57.5M in development milestones
Pivotal	2021	IPO	Reneo	Series B of $95M in Dec 2020 with Novo, Abingworth, NEA; IPO MC of $300M
Phase 1	2023	Public to Private	Cylerion/ Tisento	Mito assets moved into private NewCo with $81M financing (Venrock)

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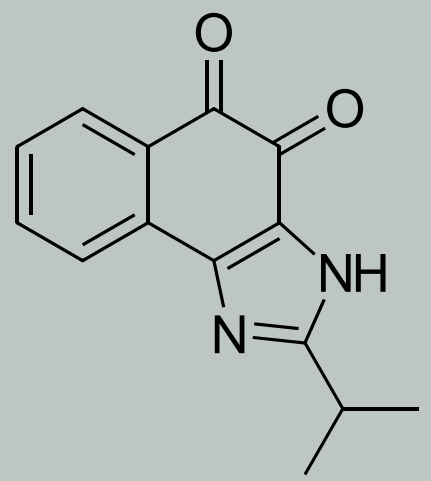
The portfolio is protected and expedited with a strong regulatory and IP package



KL1333 structure

- KL1333 (NAD^+ modulation)
  - Orphan Drug Designation in US, EU
  - Fast Track designation in US
  - Composition of matter patent until at least 2034
  - Expansion of protection ongoing
- NV354 (succinate prodrug)
  - Orphan Drug Designation in US
  - Composition of matter and use patents including in most territories until 2035
  - NV354 compositions and use patent filed 2020
  - US patent received in Feb 2023 protecting isolated forms of NV354
- Cyclosporin formulation for intravenous infusion
  - CREMOPHOR®-free emulsion decreasing risk of anaphylactic reactions until 2031
- Sanglifehrin-based non-immunosuppressive cyclophilin inhibitors (NV556)
  - Composition of matter, methods of production and use until 2031-2037

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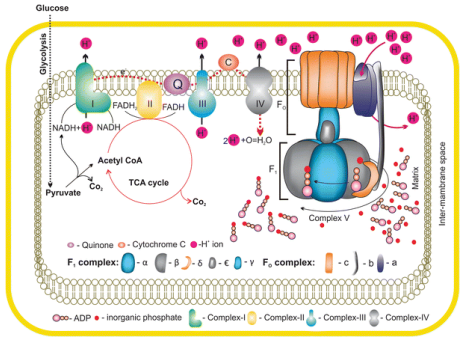
The environment now supports development in this large rare disease

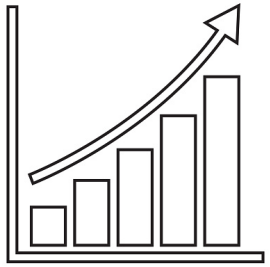
Increased Scientific Understanding



Numerous Regulatory Tools

- ODD
- PRDV
- FTD
- BT

Organized Patients & Centers



UNITED MITOCHONDRIAL DISEASE FOUNDATION.

LHON EYE SOCIETY

imp international mito-patients

Lily

Strong Internal Position

- First-in-class
- In-line with competition
- Strong patent estate

Decreased risk, decreased time to market, decreased costs to market

=

Increased commercial opportuntity

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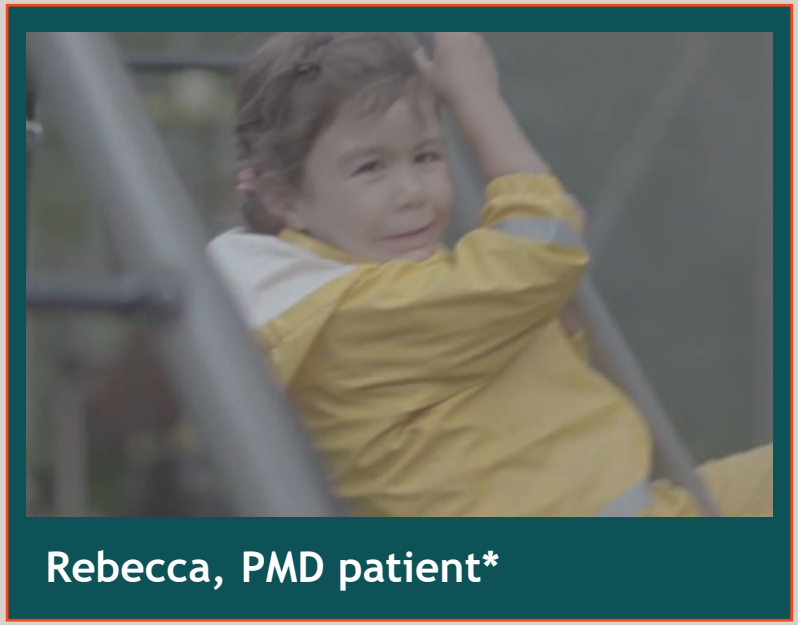
What are primary mitochondrial diseases?



Rebecca, PMD patient*

- Devastating, rare diseases with severe symptoms and continuous deterioration
  - Affects 1 in 5,000 individuals
- Impaired mitochondrial function is caused by mutations in mitochondrial (80%) or nuclear (20%) DNA
- No approved medicines for systemic PMD
- Patients experience multi-systemic complications, reduced quality of life and significantly reduced lifespan in severe cases
  - **Low NAD+/NADH ratio at root of disease**

* https://abliva.com/primary-mitochondrial-diseases/patients/

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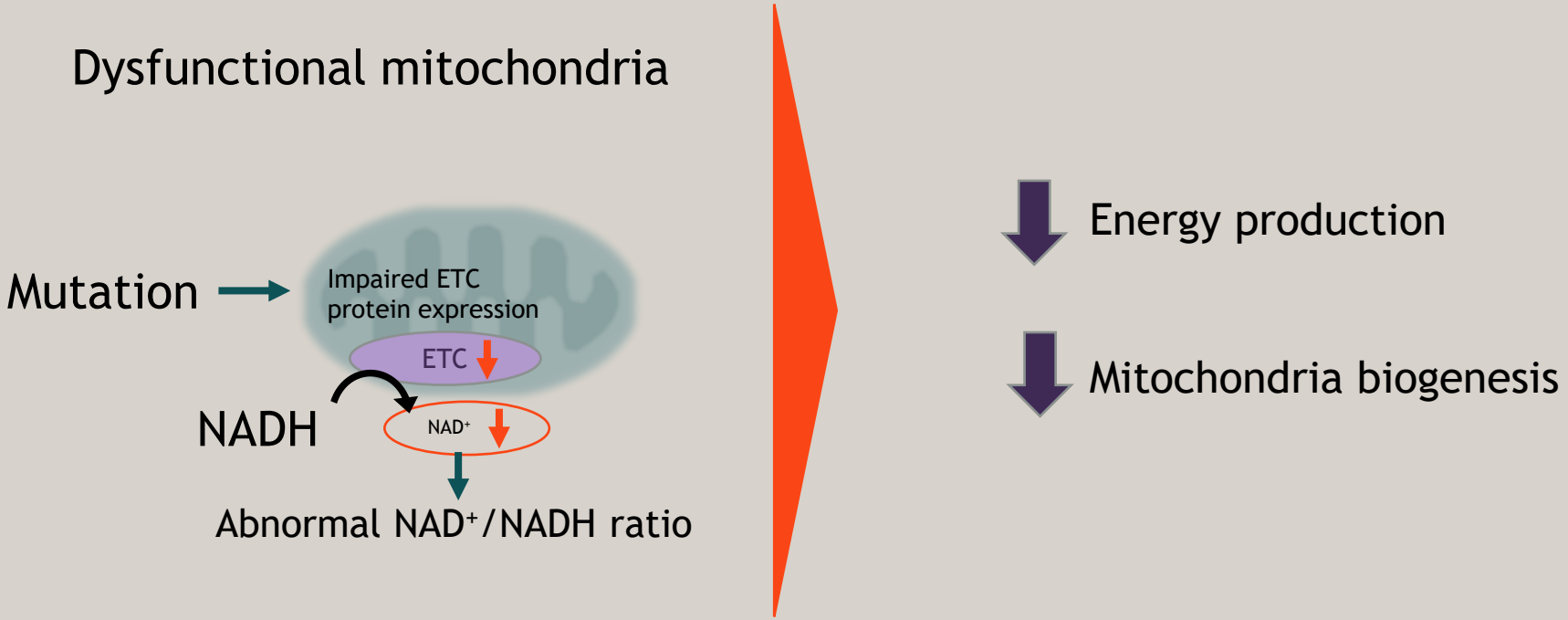
Dysfunctional mitochondria have a disrupted ratio of NAD+/NADH



Result? Lack of energy followed by organ dysfunction and disease deterioration

NAD= Nicotinamide adenine dinucleotide, NQO1= NAD(P)H quinone dehydrogenase oxidoreductases 1, ETC=Electron Transport Chain

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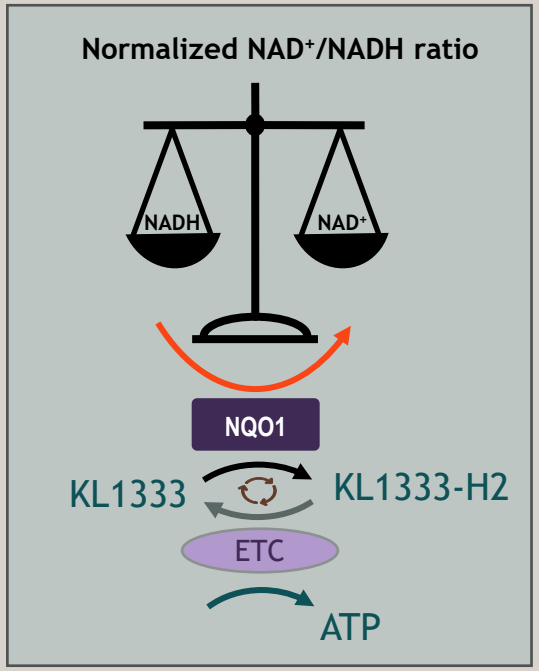
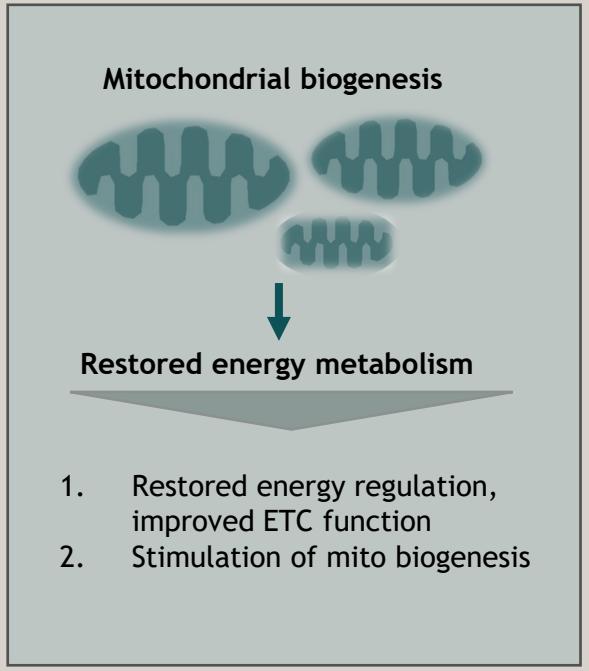
KL1333 corrects underlying pathophysiology of mito disease





Symptom Reduction

Disease Modification

Best Primary Endpoint?
Ask the patients…

NAD= Nicotinamide adenine dinucleotide, NQO1= NAD(P)H quinone dehydrogenase oxidoreductases 1, ETC=Electron Transport Chain

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Fatigue is the most common complaint of PMD patients.

"Chronic fatigue contributes to not being able to maintain employment from both physical and mental exhaustion"

-PMD Patient

"I started missing work because I was too exhausted to even get up to use the rest room."

-PMD Patient

"Just do not have enough energy for normal activities."

-PMD Patient

Study of 48 patients in 10 national centers in the US found:

- *"fatigue is very common amongst patients with PMD, with 71-100% of patients reporting fatigue*
- *…the severity of fatigue correlates with the severity of mitochondrial disease…"*

Study of 132 patients in a specialist outpatient clinic in the UK found:

- "Fatigue was common … with **64%** of patients reporting **excessive symptomatic fatigue**"
- Correlated with disease burden (NMDAS), but independent of genotype

Table 2
The rank frequency of fatigue severity as assessed by FIS (Fatigue Impact Scale).

FIS Rank	FIS descriptive	FIS scoring	Results (n=)
0	No fatigue	0–10	16
1	Mild	10–37	31
2	Moderate	38–79	43
3	Severe	80–119	38
4	Very severe	129–160	4

Energy in Action
MITOCHONDRIAL DISEASE EXTERNALLY-LED PATIENT-FOCUSED DRUG DEVELOPMENT MEETING
MARCH 29, 2019 | HYATTSVILLE, MD

Q: What mitochondrial disease symptoms most impact the patient's daily quality of life?*

- Muscle weakness (78%)
- Chronic fatigue (77%)
- Gastrointestinal problems, pain (52%)

Q: Which ability or symptom would you rank as the most important for a possible drug treatment today (select up to 3)?*

- Reduction in chronic fatigue (68%)
- Reduction in muscle weakness (57%)
- Reduced pain (35%)

1. UMDF. Energy in Action – Voice of the Patient Report. https://www.umdf.org/wp-content/uploads/2020/11/UMDF-EL-PFDD-Meeting-VOP-Report_v2019-12-03-JRG.pdf; 2. UMDF. Energy in Action – Voice of the Patient Report Transcript. UMDF-EL-PFDD-Meeting-Transcript_final.pdf. 3. UMDF. Energy in Action – Voice of the Patient Post-Meeting Online Survey Results. EL-PFDD-VOP-Report_Online-Survey-Data_Appendix-1.pdf (umdf.org).

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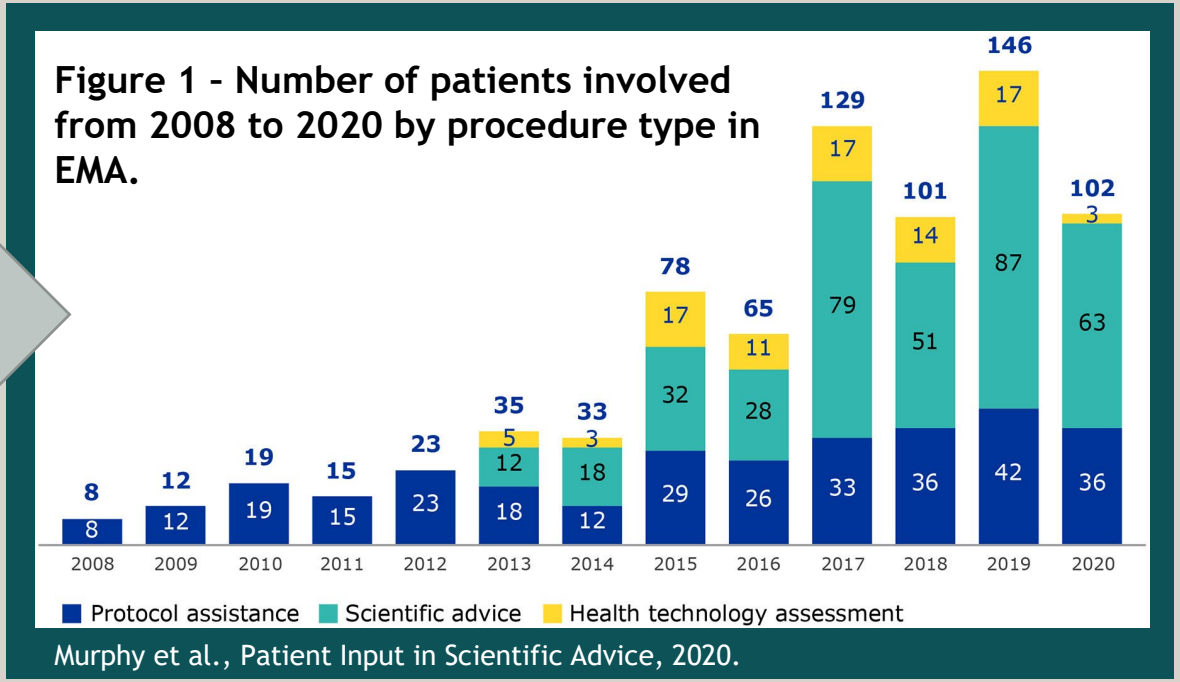
Regulators have recognized the importance of patient input into clinical design

Countless examples including:

- FDA Patient-Focused Drug Development guidance documents
- FDA Voice of the Patient
- EMA public hearings
- Patient Representative Programs
- EMA management board
- EMA Patients and Consumer Working Party (PCWP)
- FDA Patient Engagement Collaborative
- Patient review of public docs (package leaflets, safety communications, medicines summaries)
- Input in scientific advice meetings



https://www.fda.gov/drugs/development-approval-process-drugs/fda-patient-focused-drug-development-guidance-series-enhancing-incorporation-patients-voice-medical

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And have supported the use of patient reported outcome (PRO) measures

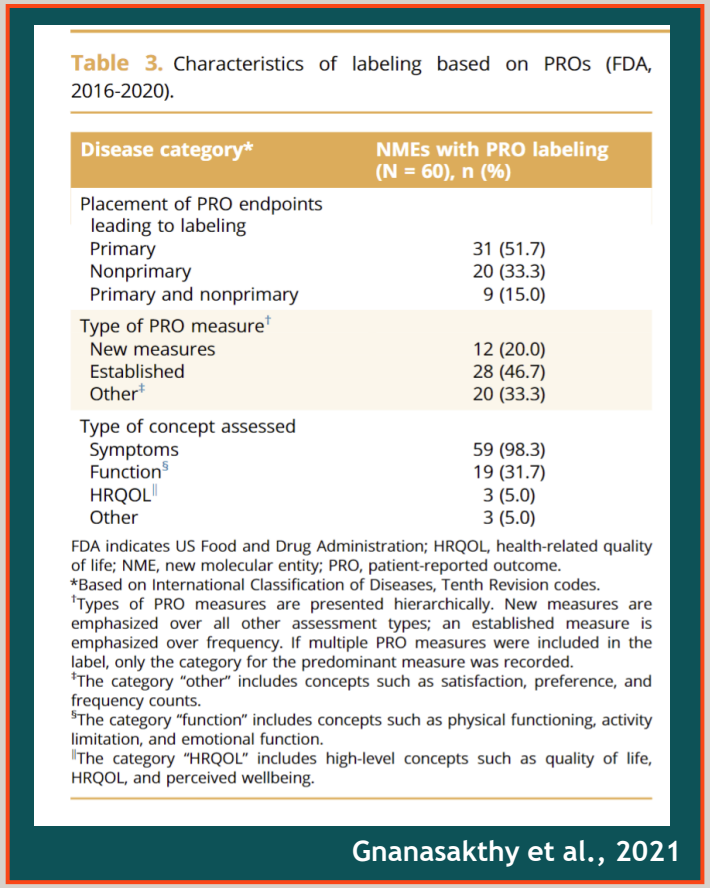

Table 3. Characteristics of labeling based on PROs (FDA, 2016-2020).

Disease category*	NMEs with PRO labeling (N = 60), n (%)
Placement of PRO endpoints leading to labeling	
Primary	31 (51.7)
Nonprimary	20 (33.3)
Primary and nonprimary	9 (15.0)
Type of PRO measure[†]	
New measures	12 (20.0)
Established	28 (46.7)
Other[‡]	20 (33.3)
Type of concept assessed	
Symptoms	59 (98.3)
Function[§]	19 (31.7)
HRQOL[‖]	3 (5.0)
Other	3 (5.0)

FDA indicates US Food and Drug Administration; HRQOL, health-related quality of life; NME, new molecular entity; PRO, patient-reported outcome.
*Based on International Classification of Diseases, Tenth Revision codes.
[†]Types of PRO measures are presented hierarchically. New measures are emphasized over all other assessment types; an established measure is emphasized over frequency. If multiple PRO measures were included in the label, only the category for the predominant measure was recorded.
[‡]The category "other" includes concepts such as satisfaction, preference, and frequency counts.
[§]The category "function" includes concepts such as physical functioning, activity limitation, and emotional function.
[‖]The category "HRQOL" includes high-level concepts such as quality of life, HRQOL, and perceived wellbeing.

Gnanasakthy et al., 2021

- **What is a PRO?** "Any report of the status of a patient's health condition that comes directly from the patient"[1]
- **What do they assess?** Symptoms, functional outcomes, quality of life aspects, treatment satisfaction
- **Are they being used?**
  - In 2004 – 2007 they were used in 14% of clinical trials[2]
  - By 2016 – 2020, use had increased to 26.3% of NDAs and 66.7% were based on primary endpoints related to the PROs[3]

(1) US FDA Guidance for industry: patient-reported outcome measures; (2) Mercieca-Bebber et al., 2018; (3) Gnanasakthy et al., 2021.

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PROM as primary endpoints are supported by several precedents across a spectrum of diseases

PROs as Key Evidence

- Tocilizumab (Jakafi®) (PROMIS)
- Solriamfetol (RINVOQ®) (FACIT)
- Sarilumab (Kevzara®) (HAQ-DI)
- Tafamadis (Vyndaque®l) (Norfolk QOL-DN)
- Tadalafil (Cialis®) (IPSS)

Fatigue PRO as Primary Endpoint

- Tocilizumab (Actemra®)
- Solriamfetol (Sunosi®)

Approval Based on PRO

- Mitoxantrone (Novantrone®)

Mitoxantrone (J. Clin Oncol. 1996; J Clin Oncol. 1999); Novantrone FDA label https://www.accessdata.fda.gov/drugsatfda_docs/label/2010/019297s033s034lbl.pdf); FDA Jakafi label https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/202192Orig1s019Rpllbl.pdf. FDA RINVOQ label https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/211675s000lbl.pdf; Actemra PI https://www.gene.com/download/pdf/actemra_prescribing.pdf

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Payers also confirmed a Fatigue PROM as a primary endpoint was “compelling”, acceptable and appropriate

PRO AS A PRIMARY ENDPOINT

- All the KOLs and Payers stated that the use of a PRO as a primary endpoint is considered acceptable and appropriate
- Payers stated that the choice of the primary endpoint would likely not pose reimbursement challenges for KL1333

FATIGUE PRO BASED ON PROMIS SHORT-FORM

- ayers had a positive view of the custom PROMIS fatigue short form; using a robust, validated tool gave them more confidence
- Some Payers commented that they were familiar with PROMIS measures as they have been used in other therapy areas
- Reaching the MCID threshold, would be considered satisfactory for KOLs and Payers, however a gap was identified regarding the translation of the T score into tangible clinical benefit
- Payers require some education on the patient burden of fatigue in PMD patients to maximise the value of KL1333

I would say the primary endpoint is compelling

- IT Payer

So the fact that it’s measured using a PROMIS fatigue short form gives it a lot of credibility. PROMIS is a rigorous, validated instrument.

- UK Payer

Fatigue PRO, in a placebo-controlled trial…yes, go ahead. For the transparency committee this is fully acceptable. But for non-HTA Payers, it may be more challenging; probably see it as subjective

- FR Payer

Source: Abliva Payer research with Access Infinity, May 2021

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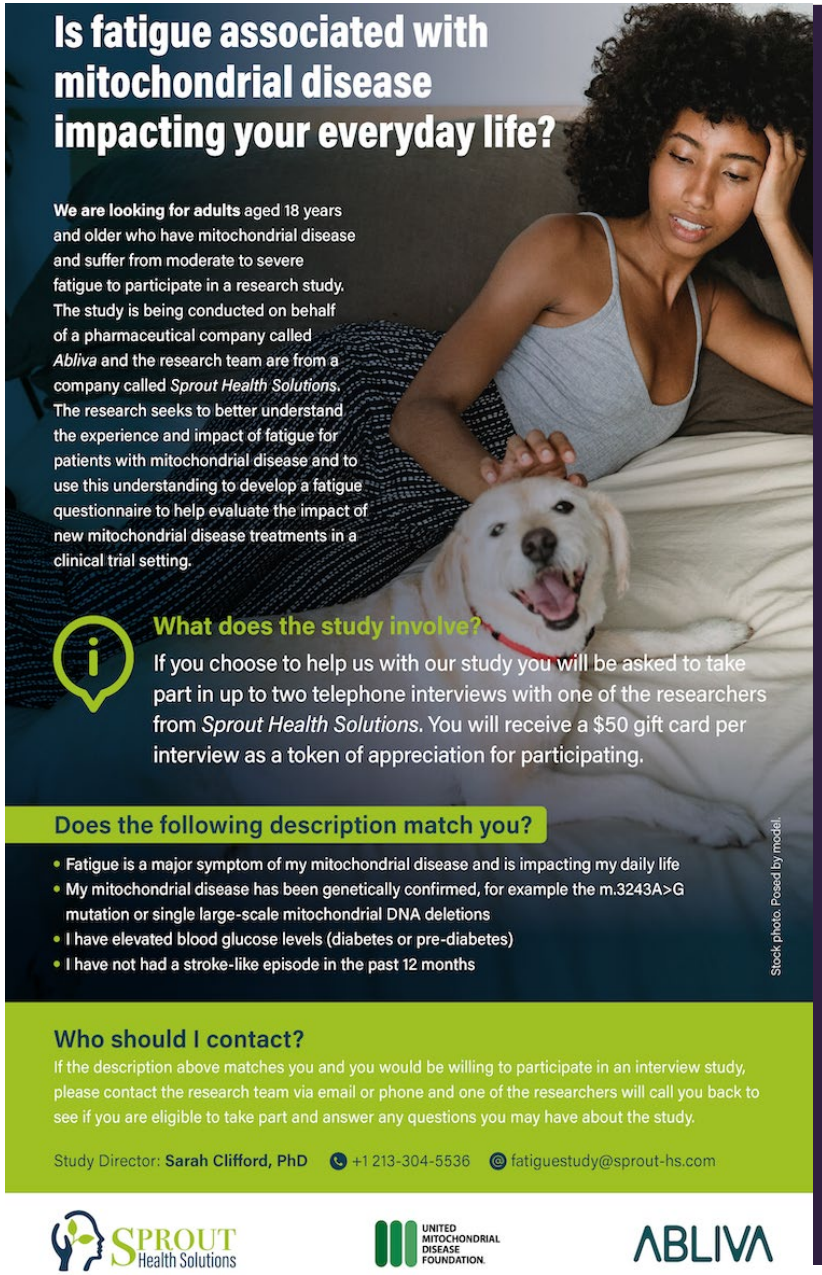
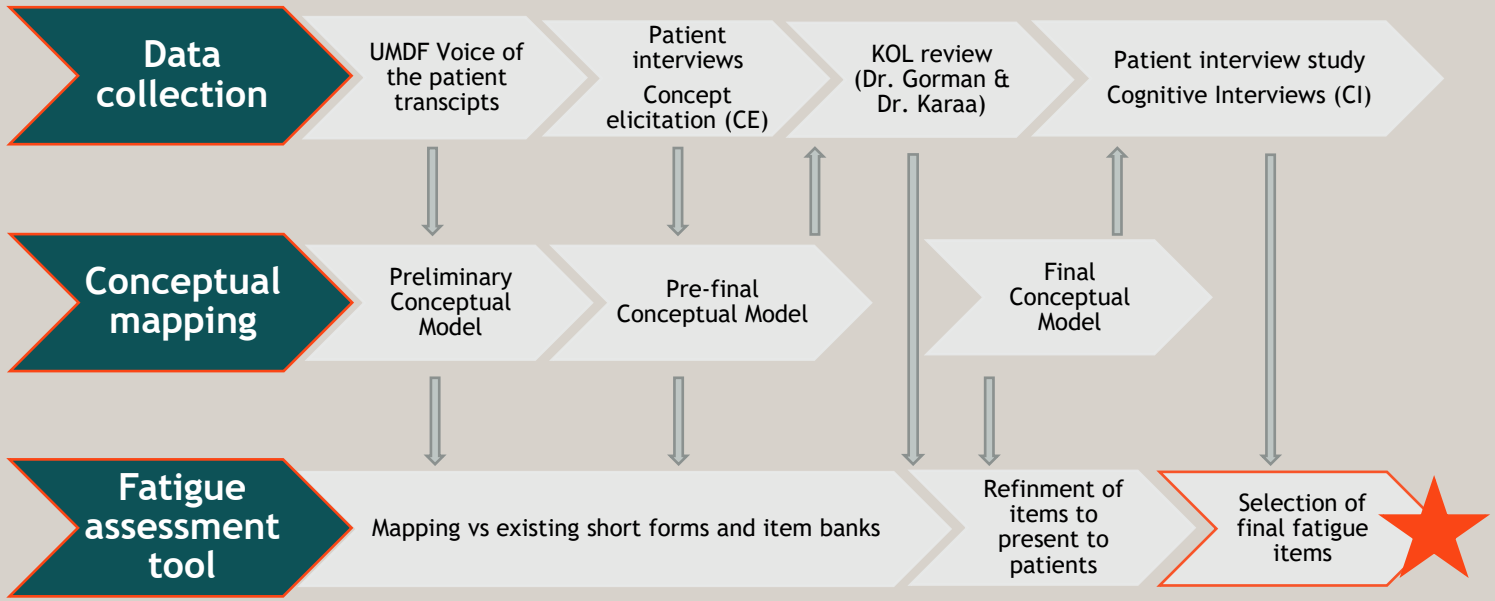


Fatigue patient study validated a fatigue ePRO specifically relevant to PMD patients



★ PROMIS® Fatigue Mitochondrial Disease Short Form

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PROMIS® Fatigue Mitochondrial Disease Short Form

	In the past 7 days…	Never	Rarely	Sometimes	Often	Always
FATEXP5	How often did you experience extreme exhaustion?	☐	☐	☐	☐	☐
FATEXP18	How often did you run out of energy?	☐	☐	☐	☐	☐
FATEXP20	How often did you feel tired?	☐	☐	☐	☐	☐
FATEXP26	How often were you too tired to enjoy life?	☐	☐	☐	☐	☐
FATIMP3	How often did you have to push yourself to get things done because of your fatigue?	☐	☐	☐	☐	☐
FATIMP19	How often were you too tired to do your household chores?	☐	☐	☐	☐	☐
FATIMP21	How often were you too tired to take a bath or shower?	☐	☐	☐	☐	☐
FATIMP29	How often were you too tired to leave the house?	☐	☐	☐	☐	☐
FATIMP30	How often were you too tired to think clearly?	☐	☐	☐	☐	☐

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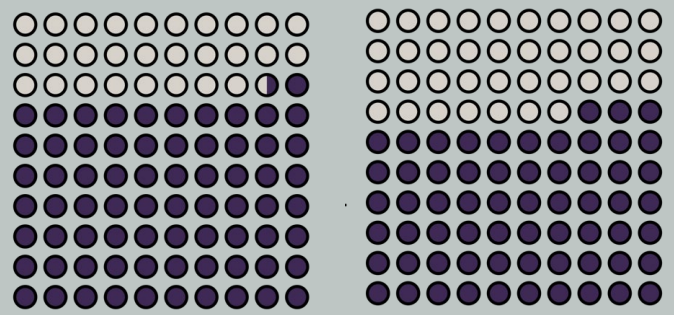
Myopathy, a frequent complaint of patients, will be evaluated as alternative primary endpoint

Frequency confirmed by registry study

Abliva study of UK PMD registry (>500 adults with active entries past 3 years):

Exercise Intolerance	Proximal muscle weakness



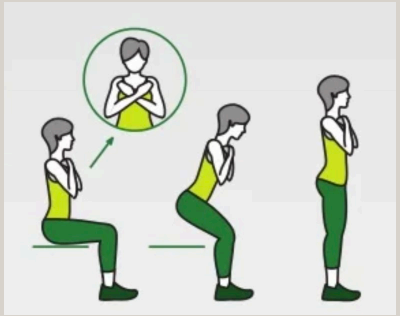
Importance confirmed by patients in Voice of the Patient Report

"Something that makes my muscles stronger would have a huge impact."
-PMD Patient 1

"I am afraid of what the progressive muscle weakness will do to me, not being able to care for myself is a concern."
-PMD Patient 2

"So many of the other symptoms would be tolerable if the fatigue, muscle weakness and pain were addressed."
-PMD Patient 3

30 second Sit-to-Stand



1. UMDF. Energy in Action – Voice of the Patient Report. https://www.umdf.org/wp-content/uploads/2020/11/UMDF-EL-PFDD-Meeting-VOP-Report_v2019-12-03-JRG.pdf; *2. UMDF. Energy in Action – Voice of the Patient Report Transcript.* UMDF-EL-PFDD-Meeting-Transcript_final.pdf. 3. UMDF. Energy in Action – Voice of the Patient Post-Meeting Online Survey Results. EL-PFDD-VOP-Report_Online-Survey-Data_Appendix-1.pdf (umdf.org). *N=260 for both questions.

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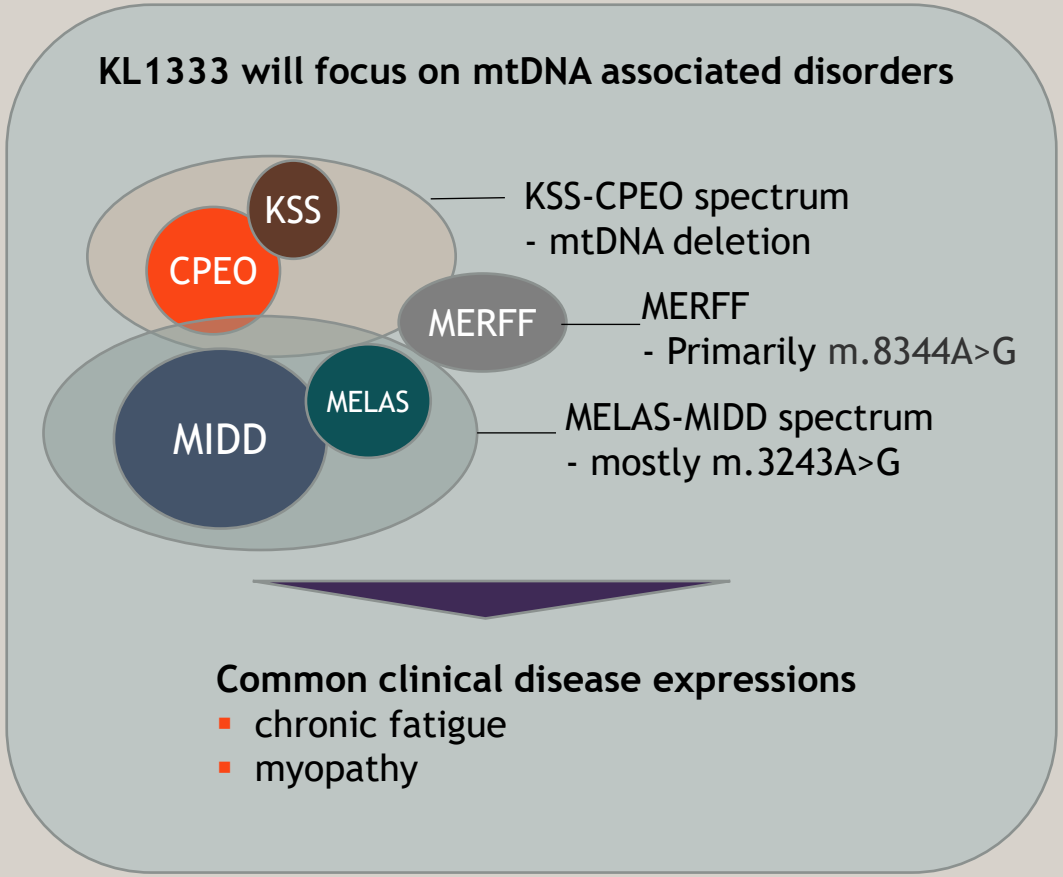
Focusing on genetically - and phenotypically-defined subgroups of PMD will improve likelihood of success



Benefits:

- Genotypes with peripheral systemic involvement providing ***greater homogeneity***
  - Category 6 of the International Classification of Inherited Metabolic Disorders (ICIMD)
- Most closely linked to preclinical evidence base
- Represent ***large percentages*** of mito disease population [1]
  - USD 1bn+ opportunity
- Validated in recent FDA feedback

1. Gorman et al Ann Neurol 2015;77:753–759

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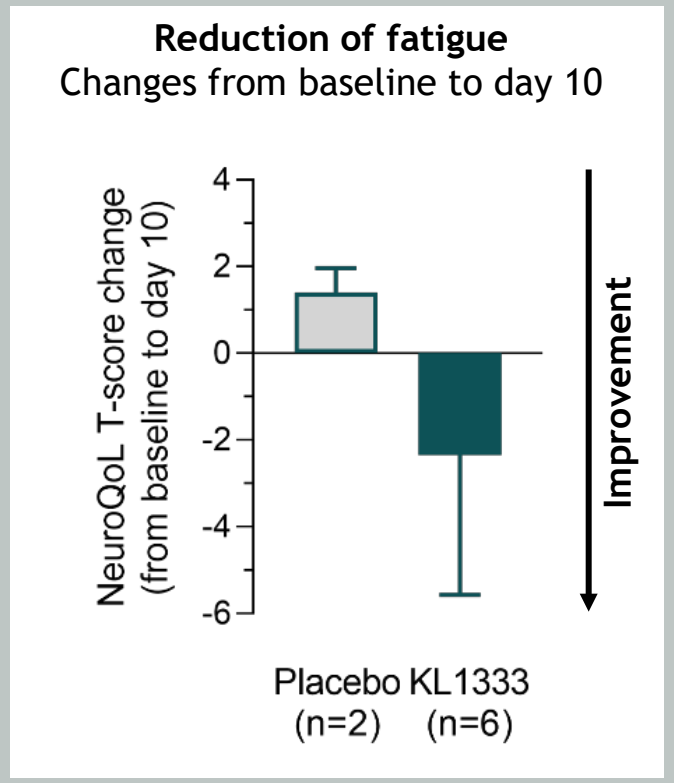
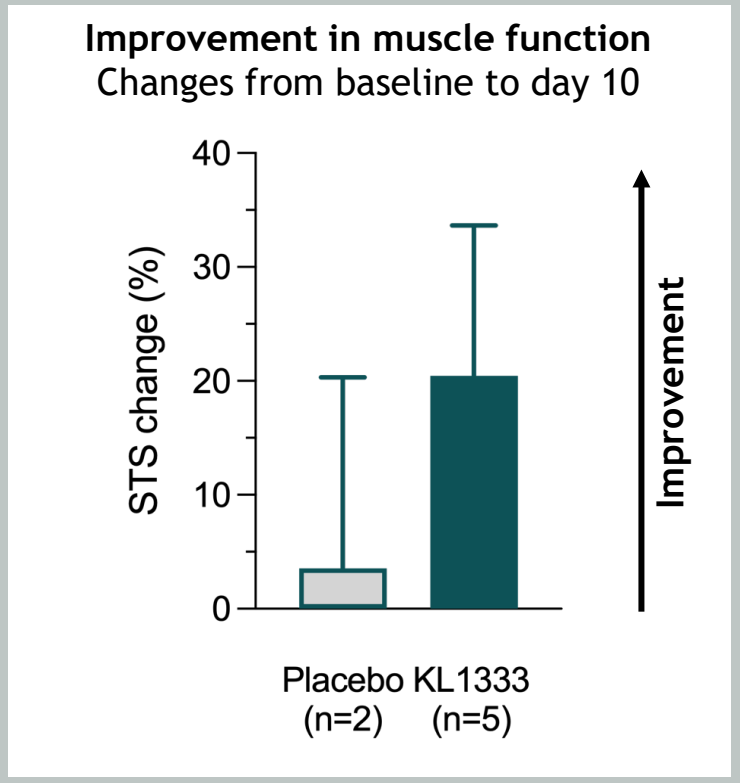
KL1333 showed signals of efficacy after 10 days, 50 mg/day in PMD patients





Phase 1b study data:

- Clinically meaningful effect signals on fatigue
- Clinically meaningful effect signals on muscle weakness and endurance
- Exposure / effect relationship
- Target engagement demonstrated

Fatigue: Minimally important differences for fatigue scales ranges from 2.5-5 in T-score (Yost et al 2011); DFIS ranges from 3-4 as extrapolated from Nordin et al. 2016. Myopathy: One subject in the KL1333 group did not perform test (excluded from analysis); Minimally important differences for 30sSTS from Wright et al 2011 (Osteoarthritis), Zanini et al. 2019 (COPD)

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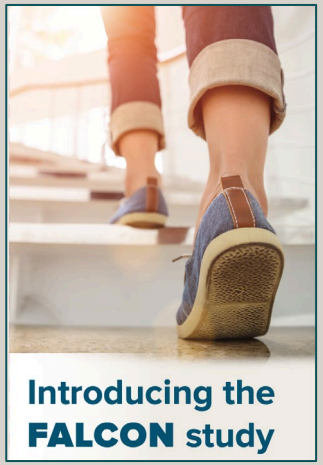
The Phase 2 FALCON study commenced in December 2022



8-12 weeks	48 weeks	5 weeks
Screening	Treatment (tablets twice daily) 40% placebo - 60% active	Follow-up

- **Design:** Randomized, double-blind, parallel-group, placebo-controlled
- **Patients:** Adult Primary Mitochondrial Disease (PMD) patients with:
  - Multisystemic mitochondrial DNA-related disease (according to category 6* of the International Classification of Inborn Metabolic Disorders)
  - Disease expressions involving at least chronic fatigue and mitochondrial myopathy/exercise intolerance
- **Treatment:** Oral twice daily dosing for 12 months (including dose titration phase)
- **Size:** Adaptive platform design of 120-180 patients financed to interim analysis
- **Endpoints:**
  - Alternate Primary: Fatigue (validated for PMD*), 30 Second Sit-to-Stand
  - Secondary: Clinician- and Patient- Global Impression of Disease Severity; NMDAS**; patient-specific activity assessments

*Including MIDD-MELAS-m.3243A>G associated spectrum disease, single large scale mtDNA deletion associated KSS-CPEO spectrum disorders, MERRF, and other multisystemic mitochondrial DNA-related disease.; ** Newcastle Mitochondrial Disease Adult Scale (NMDAS) (Schaefer et al., 2006)

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FALCON study is currently on track for interim analysis mid-2024

- Expansive global network is actively screening patients
  - 18 sites activated, 18 sites screening patients
  - US, UK, France, Spain, Belgium, Denmark

- Study on track to dose approx. 40 patients (Wave 1) by end of 2023
  - Interim analysis (IA) triggered 6 months after the dosing of the 40th patient
  - IA on track for mid-2024

The team at Abliva brings wealth of experience in drug development and mitochondrial medicine

Ellen Donnelly, PhD
CEO

- Formerly CEO of Modus Therapeutics (SCD focus)
- Leadership positions at Pfizer
- Corporate consulting, SVB Leerink
- PhD, Yale School of Medicine

Catharina Johannson
CFO

- Abliva CFO since 2013
- Senior financial positions in companies such as Assa Abloy, Entrematics, Bong, Alfa Laval Europe
- Interim CFO Cellavision

Magnus Hansson, MD/PhD
CMO

- Abliva since 2008; CMO since 2016
- Consultant physician at Skåne University Hospital and Associate Professor at Lund University with long experience in mitochondrial medicine development

Eskil Elmer, MD/PhD
CSO

- Co-Founder, Abliva
- Professor, Lund University
- 20+ years of research in mitochondrial medicine

Dag Nesse
VP Clin Ops

- Abliva since 2023
- Previous Head of Clin Ops at Calliditas
- 25 years of Clinical Ops incl. leadership from pivotal study to data readout, marketing authorization, and launch

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The Abliva team is supported by a strong Board and SAB

Board of Directors

- **David Laskow-Pooley**
  Director of the Board of Marker Therapeutics Inc. (England), Pharmafor Ltd, England, and LREsystem Ltd, (England).
- **David Bejker**
  Affibody Medical AB (CEO, Board), LIDDS AB (Board), Amylonix AB (Board).
- **Roger Franklin**
  Partner, Hadean Ventures
- **Denise Goode**
  QED Life Sciences Ltd (CEO, Board). 20 years with AstraZeneca in senior finance & business roles.
- **Jan Tornell**
  Innoext AB (CEO, Board), LIDDS AB (Chair), and Glactone Pharma AB (Chair), Diaprost AB (Board), LIDDS Pharma AB (Deputy Board).

Scientific Advisory Board

- **Amel Karaa, MD,PhD,** Ass. Prof, internist and medical geneticist, Dir. Mito Disease Program, Harvard, MGH. President of the Mitochondrial Medicine society.
- **Bruce Cohen, MD, PhD,** Paediatric Neurologist, Director, Neuro-Developmental Science Center, Akron
- **Michio Hirano, BA, MD, PhD,** neurologist, Columbia. Co-director the North American Mitochondrial Disease Consortium
- **Marni Falk, BS Sci, MD, PhD**, Clinical Geneticist, Associate Prof. of Pediatrics at Penn, CHOP. Advisory Board of UMDF, founding member of the CHOP Center for Mitochondrial and Epigenomic Medicine
- **Grainne Gorman, MD, PhD,** Newcastle, Neurologist, co-founder of the Wellcome Centre for Mitochondrial Research Leader of the Newcastle Mito Hub
- **Robert Pitceathly, MD, PhD,** Neurologist, Clinical Scientist, Department of Neuromuscular Diseases UCL Queen Square Institute of Neurology
- **Michelangelo Mancuso, MD, PhD,** Ass. Prof, Neurologist, Coordinator Clinical Neurogenetics and Rare Diseases, University of Pisa, Italy

KL1333

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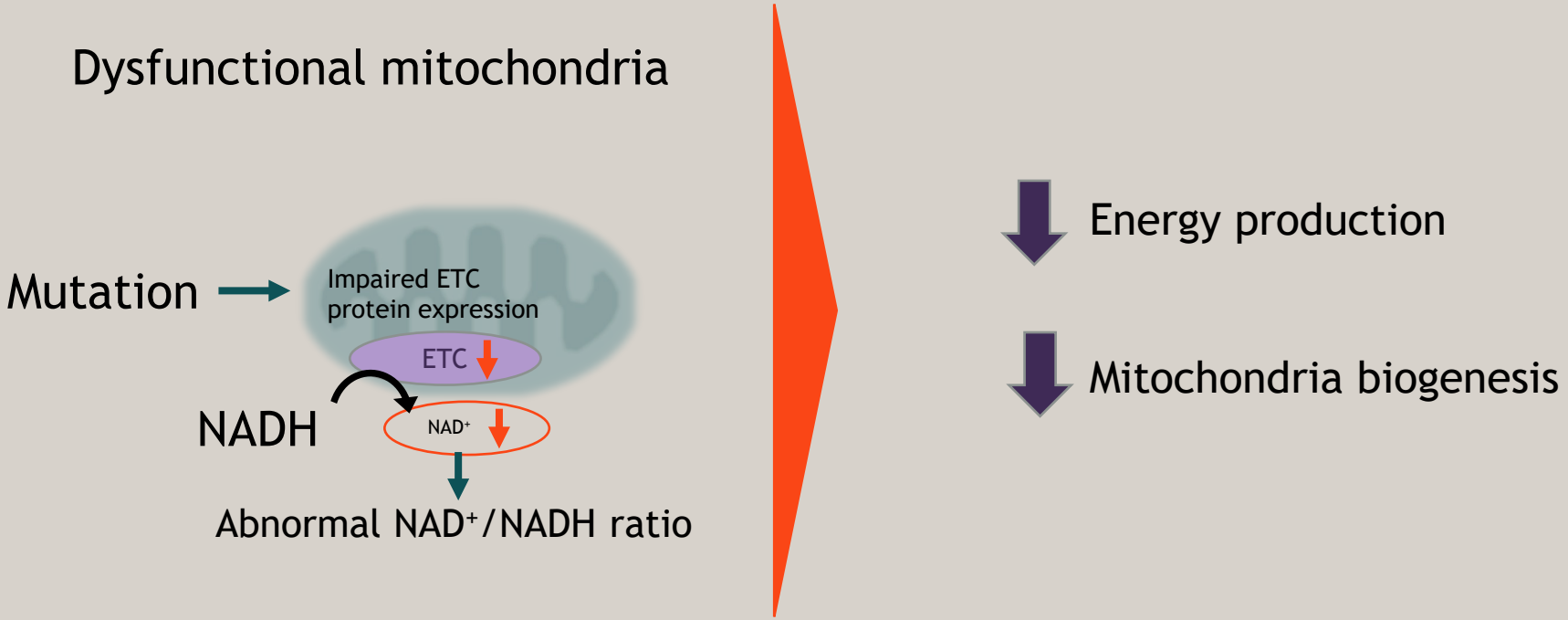
Dysfunctional mitochondria have a disrupted ratio of NAD+/NADH



Result? Lack of energy followed by organ dysfunction and disease deterioration

NAD= Nicotinamide adenine dinucleotide, NQO1= NAD(P)H quinone dehydrogenase oxidoreductases 1, ETC=Electron Transport Chain

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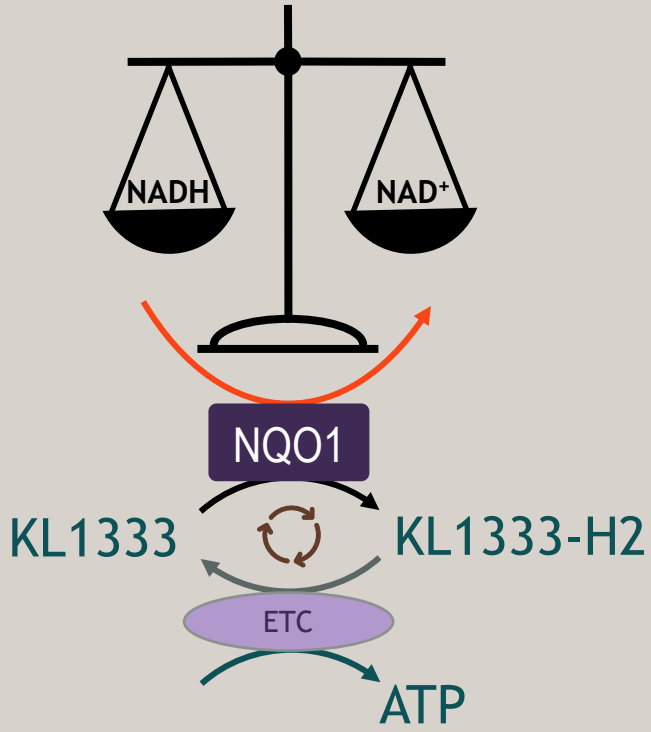
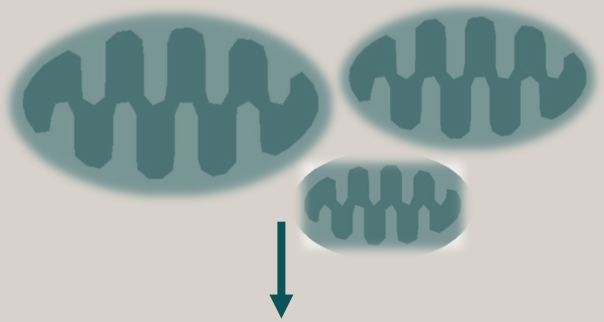
KL1333 corrects underlying pathophysiology of mito disease



Mitochondrial biogenesis



Restored energy metabolism

1. Restored energy regulation and improved ETC function
2. Mito biogenesis stimulated

Overall results: Symptom reduction, disease modification

NAD= Nicotinamide adenine dinucleotide, NQO1= NAD(P)H quinone dehydrogenase oxidoreductases 1, ETC=Electron Transport Chain

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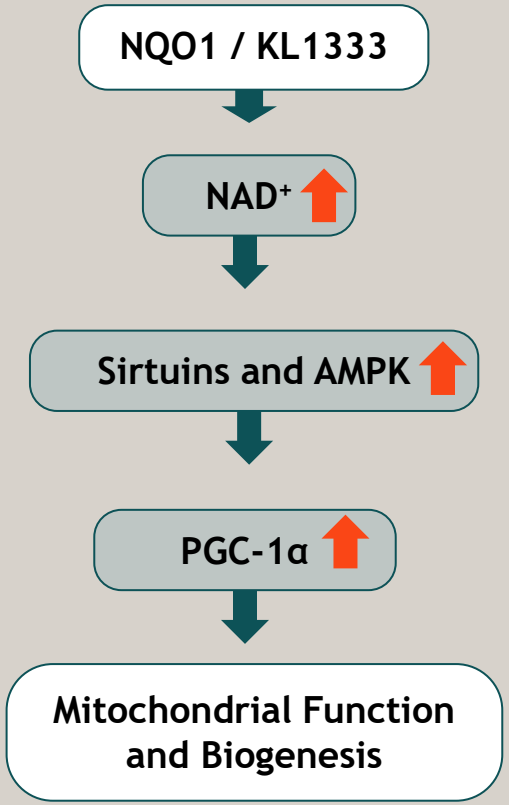
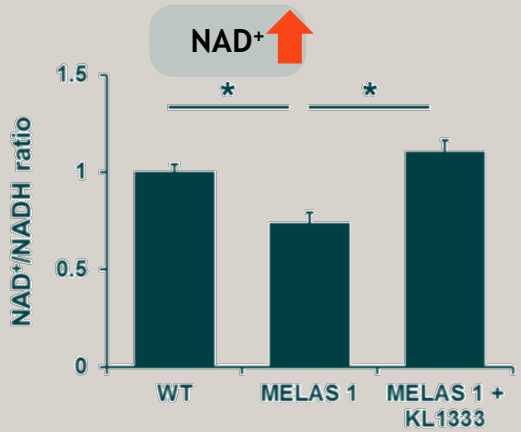
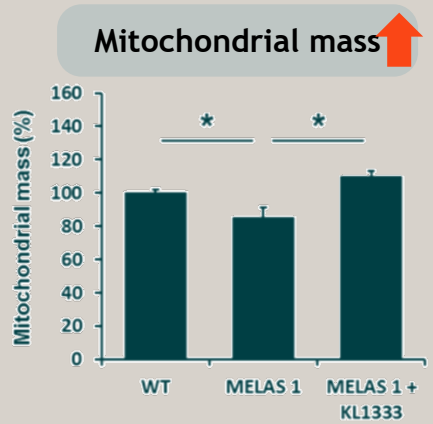
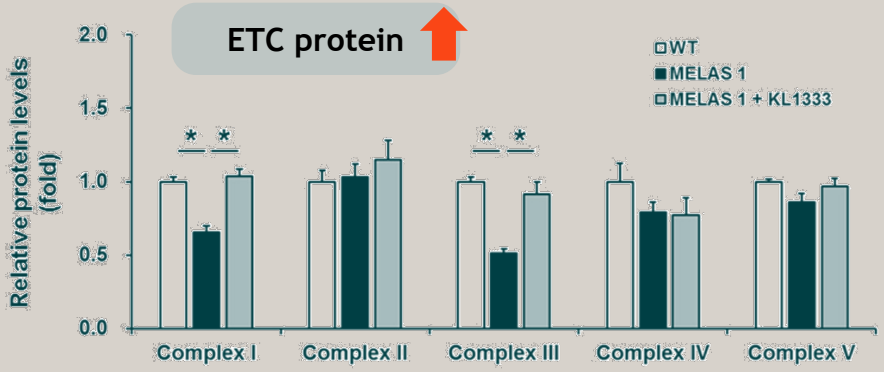
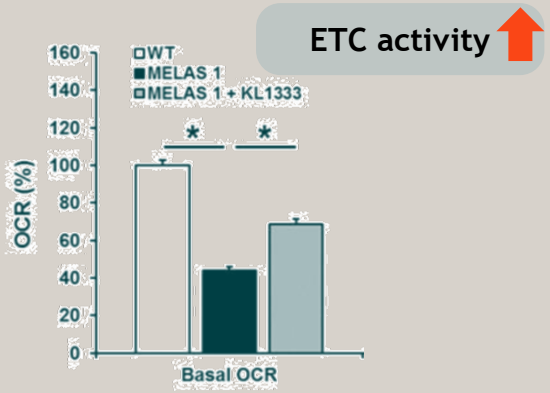
KL1333 increases NAD+ and mitochondrial biogenesis in MELAS patient fibroblasts











Seo et al. 2018. KL1333, a Novel NAD+ Modulator, Improves Energy Metabolism and Mitochondrial Dysfunction in MELAS Fibroblasts (https://www.frontiersin.org/articles/10.3389/fneur.2018.00552/)

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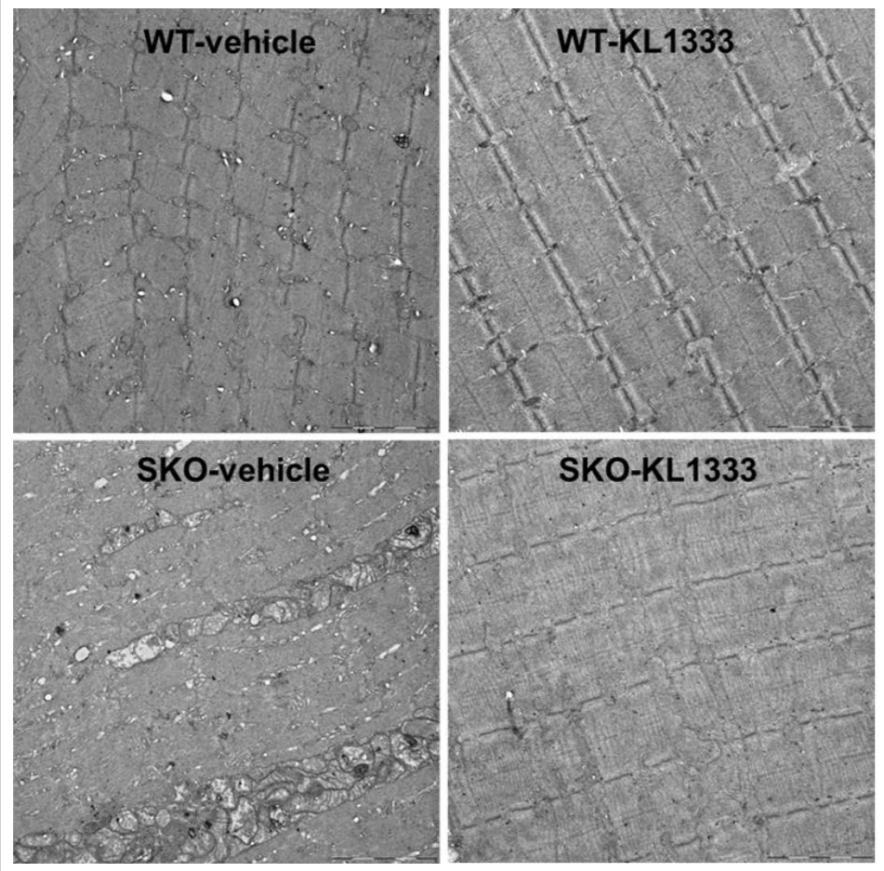
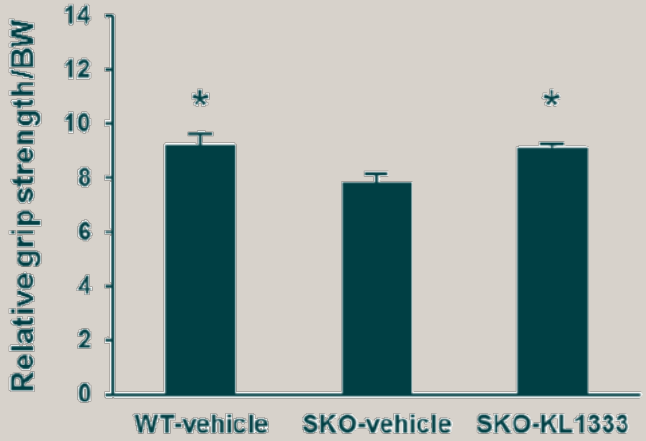
KL1333 improves muscle function and histology in an *in vivo* mouse model



- Mito disease model *Crif1* skeletal knock-out (SKO) mice have impaired translation of mtDNA-encoded respiratory chain subunits
  - Similar to m.3243A>G mutation and large mtDNA deletions



KL1333 qd oral dosing for 4 w (n=4-5/group

- **KL1333 significantly increases grip strength and normalizes muscle histology**

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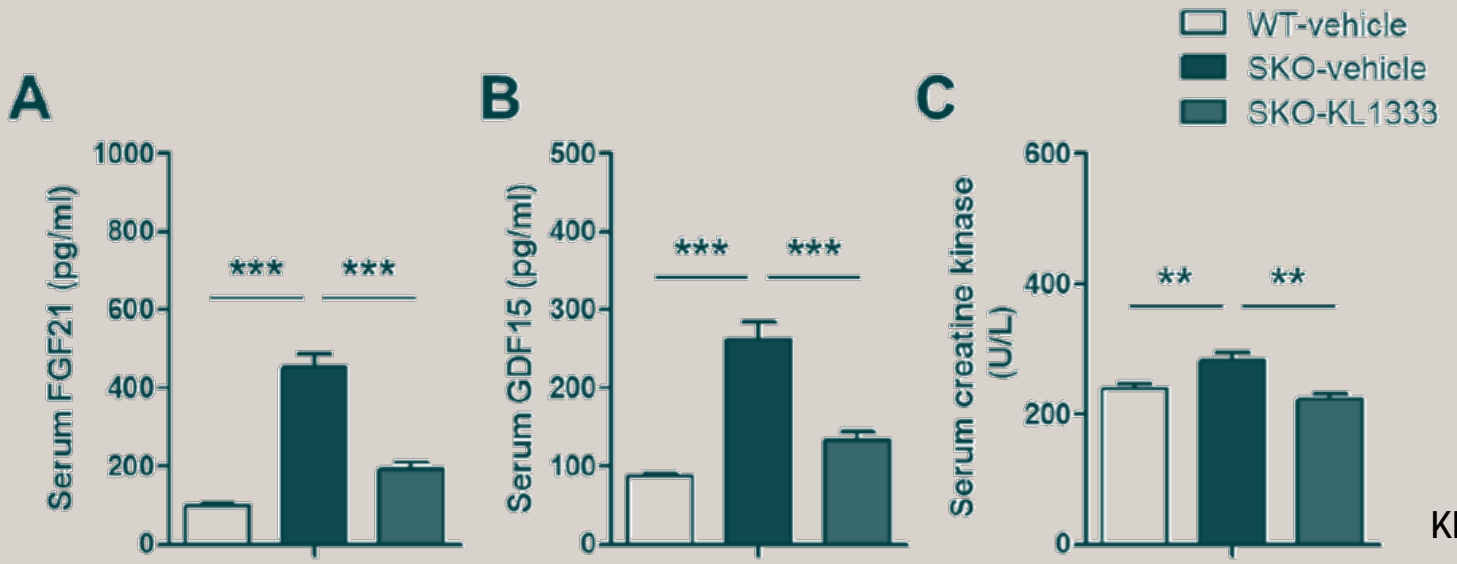
KL1333 improves mitochondrial biomarkers in an *in vivo* mouse model

Mito disease model *Crif1* skeletal knock-out mice



KL1333 qd oral dosing for 4 w (n=4-5/group)

- KL1333 significantly reduces mitochondrial disease biomarkers FGF21 & GDF15, and normalizes muscle injury marker creatine kinase

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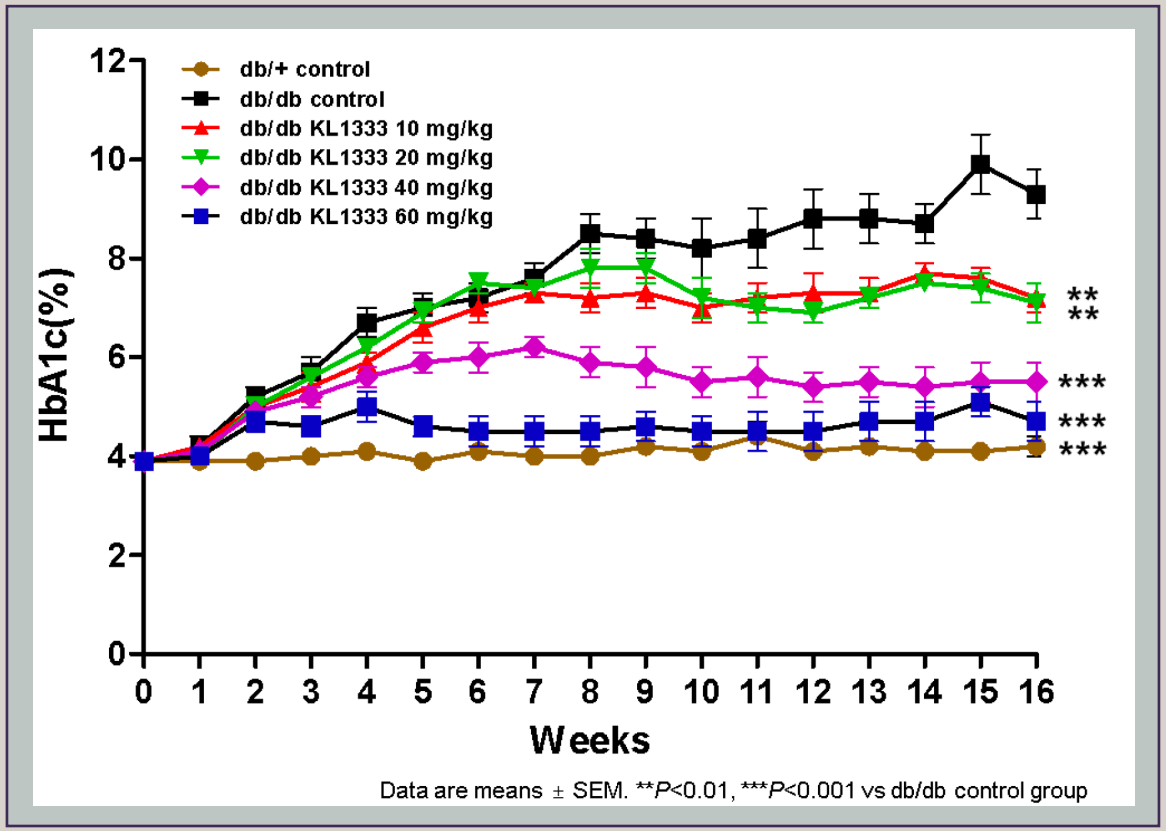
KL1333 improves established biomarker in diabetic mice



- KL1333 dose-dependent reduction in HbA1c levels in diabetic mice

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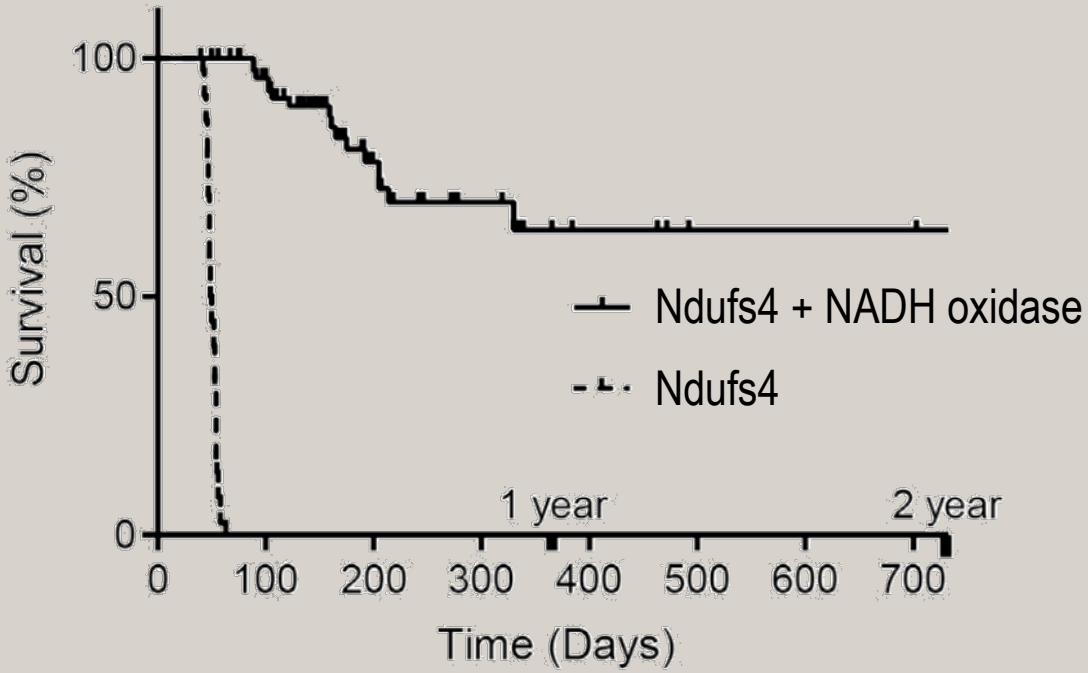
Animal model validation of NAD+/NADH correction in mito disease



- Artificial NADH oxidases raises NAD+ levels and increases lifespan in mitochondrial disease model (Ndufs4)[1]
  - Other studies show cell metabolism rescue[2] and normalization of mito disease biomarkers[3]

[1] McElroy et al. Cell Metab. 2020;32(2):301-308
[2] Titov et al. Science 2016;352(6282):231-5
[3] Goodman et al. Nature 2020;583:122–126

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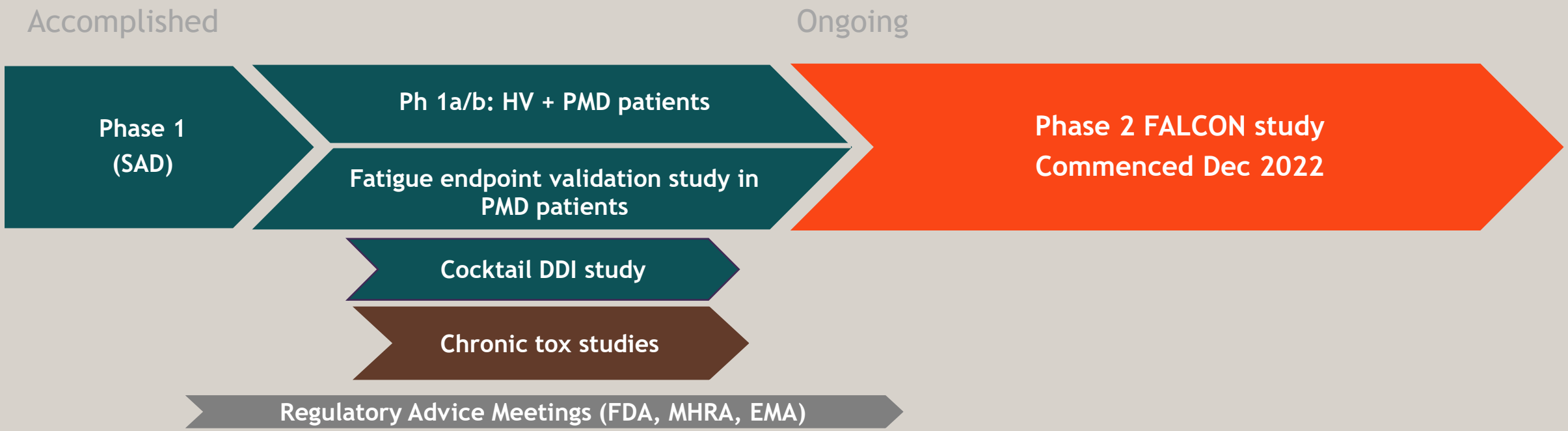
KL1333: Development Plan Overview



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KL1333 has a very attractive safety profile with no safety signals seen in previous studies

Single ascending dose study 25-800mg

- No safety signals
- Mild dose-dependent GI AEs at high doses

Drug Drug Interaction study

- KL1333 was a weak inhibitor of CYP1A2 but had negligible effects on other CYP substrates

Multiple dose study 25-250mg

+

Patient cohort

- No safety signals
- Tolerability at higher doses limited by mild-moderate GI-related side effects - improved by dividing dose
- Similar PK/safety profile in PMD patients compared to healthy volunteers
- Signals of target engagement and improvements of fatigue & myopathy

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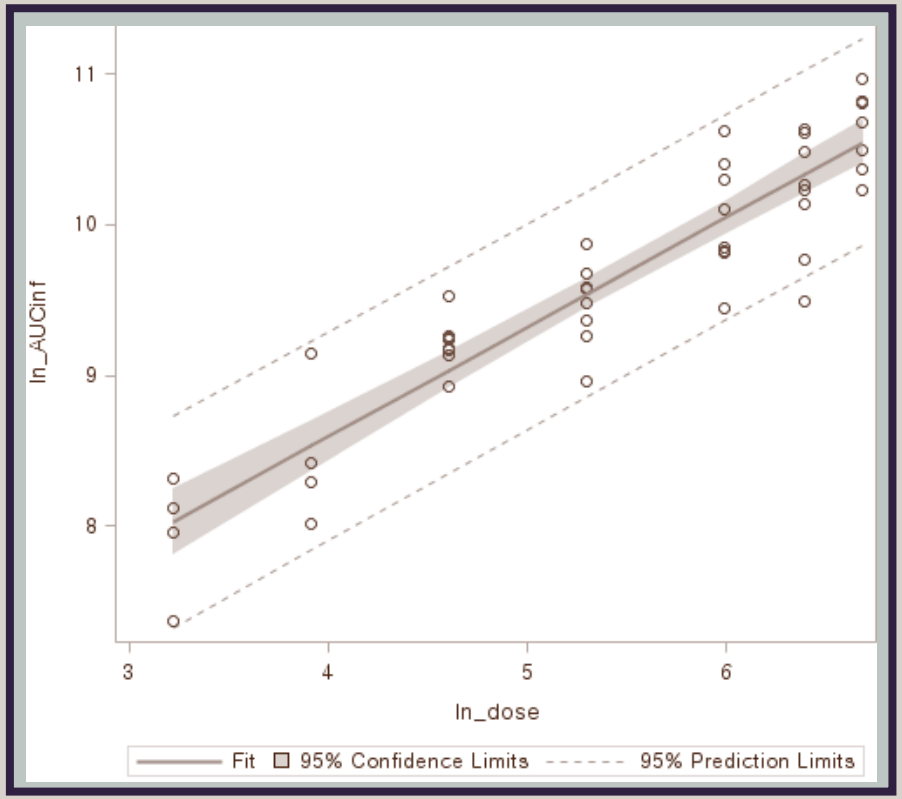
Early Phase 1 SAD study confirmed safety profile and dose-proportional exposure



- Single ascending dose study completed in Korea by partner
  - No Serious Adverse Events (SAEs), mild dose-dependent GI AEs at high doses
  - Dose-proportional exposure of KL1333

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Phase 1a/1b study design

What? A Randomised, Double-blind, Parallel-group, Placebo-controlled, Phase Ia/Ib, Multiple-site Study

Why? Assess the Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of KL1333

How? Single Oral Dose and Multiple Ascending Oral Doses

Who? Healthy Subjects and Patients with Primary Mitochondrial Disease

Study contained 4 parts, with 56 healthy volunteers and 8 PMD patients:

- Part A: SAD with Food effect, 1 cohort 25 mg QD, healthy volunteers
- Part B: MAD, 5 cohorts 25, 50, 75, 150 and 250 mg QD, healthy volunteers
- Part C: 10 days dosing, 50 mg QD, 1 cohort, PMD patients
- Part D: Split dosing (75 mg BID or 50 mg TID), 2 cohorts, healthy volunteers

Healthy volunteer cohorts began in March 2019 and were run at the Covance CRU in Leeds, UK.

Patient cohort was started in October 2020 and was run at University College London (Robert Pitceathly, Chief Investigator) and Newcastle (Grainne Gorman), UK.

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Phase 1a/1b objectives

Primary

- **Safety and tolerability of a single oral dose (**with/without food) in healthy volunteers (HVs)
- Safety and tolerability of multiple oral doses in HVs and PMD patients

Secondary

- **Single oral dose plasma pharmacokinetics (PK)** in HVs, including the effect of food intake
- **Multiple oral dose plasma PK** in HVs and PMD patients

Exploratory

- Multiple-dose PD in HVs and PMD patients using blood **biomarkers**
- **Clinician- and patient-rated outcome assessments** following multiple oral doses of KL1333 in PMD patients

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The impact of KL1333 on fatigue was assessed using two independent scales

Scales:

- Quality of Life in Neurological Disorders (Neuro-QoL) Short Form (SF) Fatigue
- Daily Fatigue Impact Scale (D-FIS)

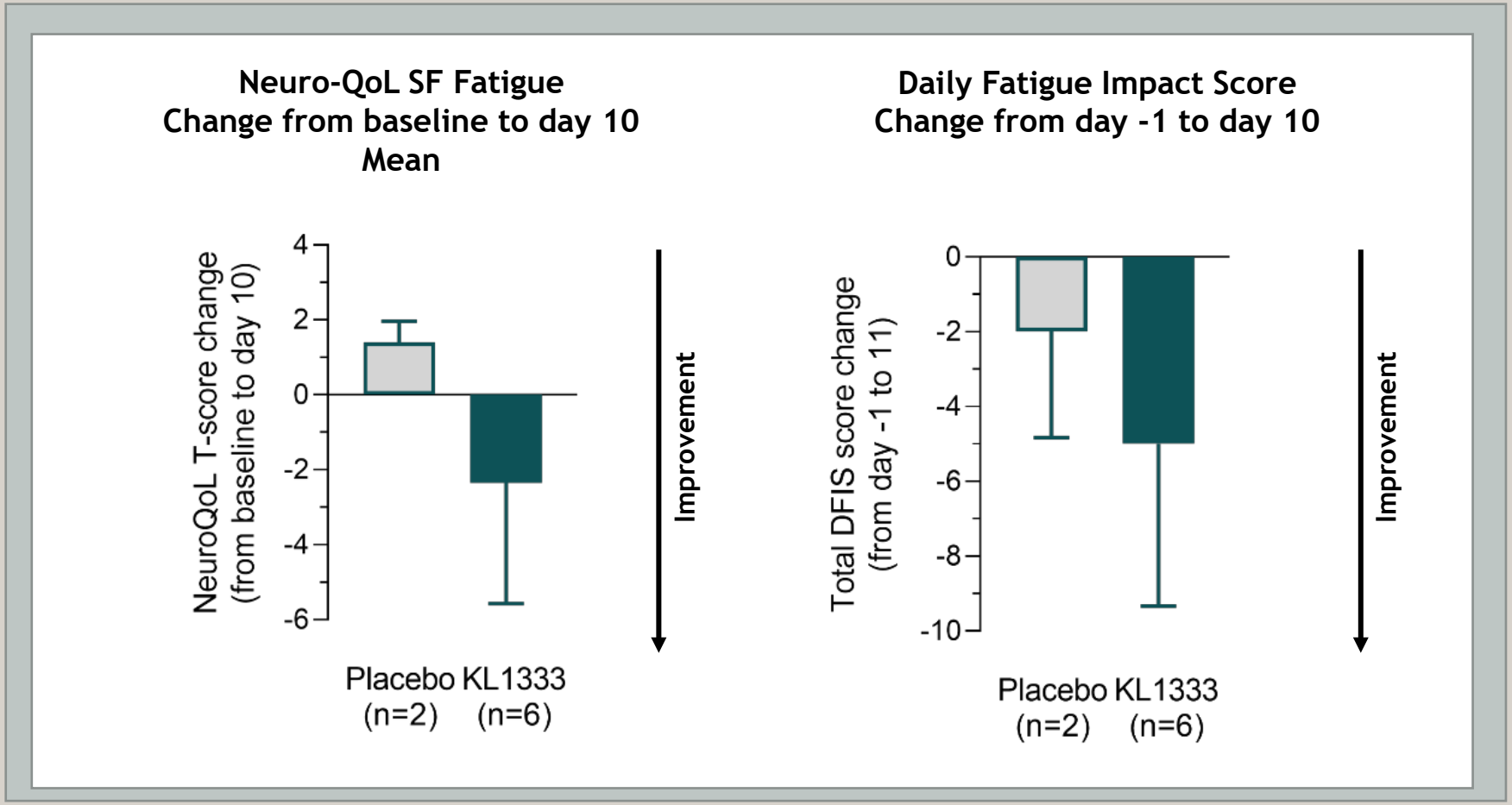
Relevance:

- Fatigue is critically important to patients
- Fatigue endpoint is supported by the FDA
- Neuro-QoL fatigue (used in Phase 1b) is equivalent to the PMD-specific form validated by Abliva and included in the ongoing Phase 2 study

Neuro-QoL Short Form Fatigue

In the past 7 days…	Never	Rarely	Sometimes	Often	Always
I felt exhausted……	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
I felt that I had no energy……	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
I felt fatigued……	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
I was too tired to do my household chores.	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
I was too tired to leave the house……	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
I was frustrated by being too tired to do the things I wanted to do……	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
I felt tired……	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
I had to limit my social activity because I was tired……	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

Patients given KL1333 showed a marked improvement in fatigue with only 10 days of dosing



Minimally important differences for fatigue scales ranges from 2.5-5 in T-score (Yost et al 2011); DFI-S ranges from 3-4 as extrapolated from Nordin et al. 2016.

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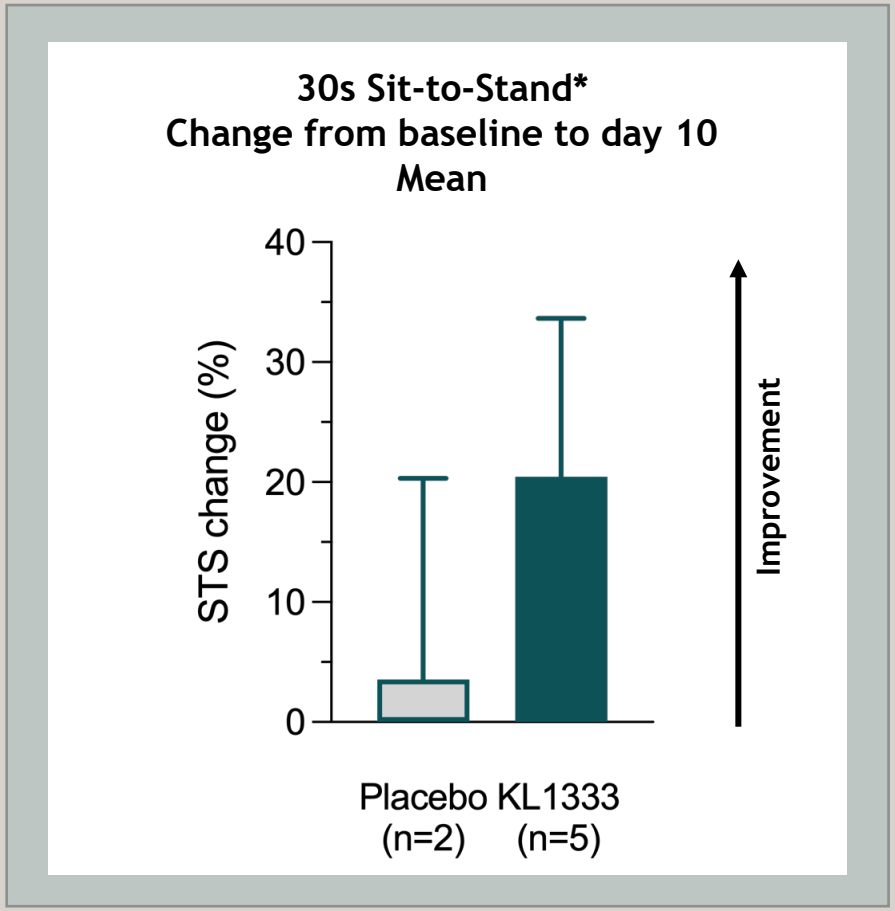
The 30 sec Sit-to-Stand endpoint also showed signs of efficacy in mitochondrial disease patients



Notes on Sit-to-Stand:

- Score = number of repetitions (higher score = better muscle strength/endurance)
- ≥2 repetitions has been defined as the minimum clinically important difference in osteoarthritis and COPD**

* One subject in the KL1333 group did not perform test (excluded from analysis)

**Wright et al 2011 (Osteoarthritis), Zanini et al. 2019 (COPD)

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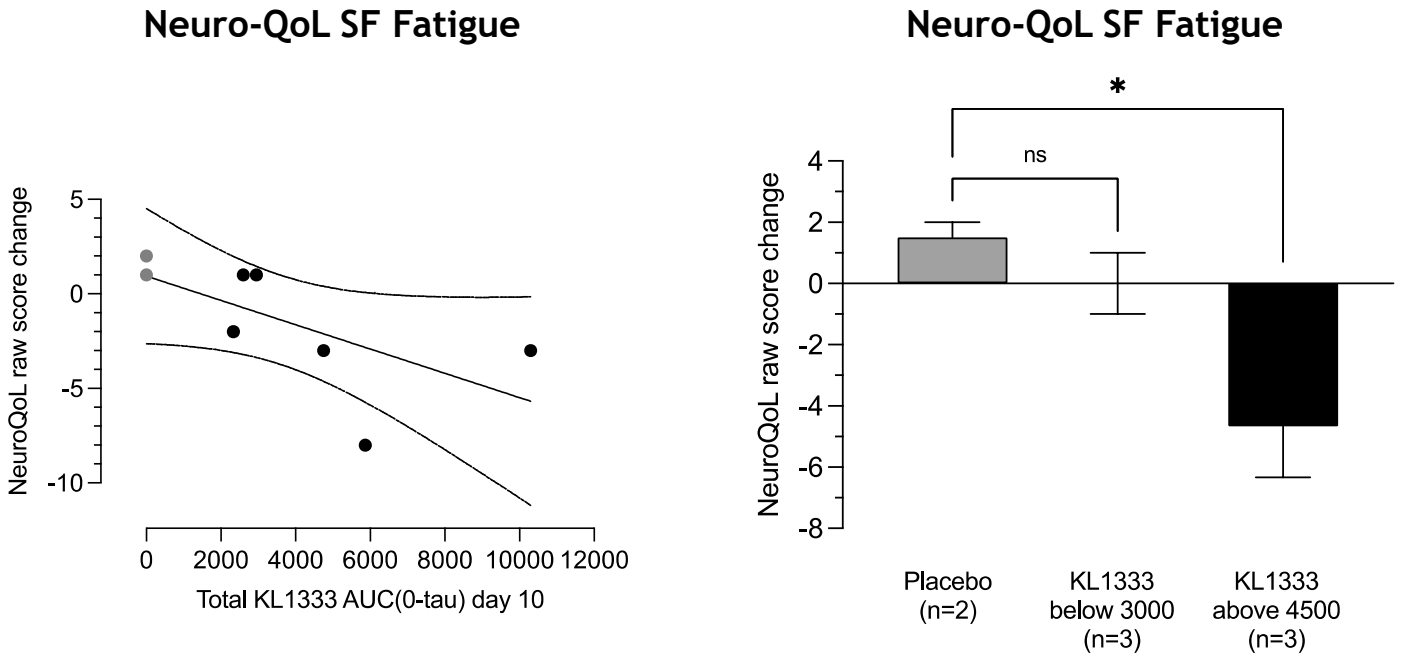
Exposure and effect were correlated across all clinical outcome measures

Reduction of fatigue in relation to exposure of KL1333



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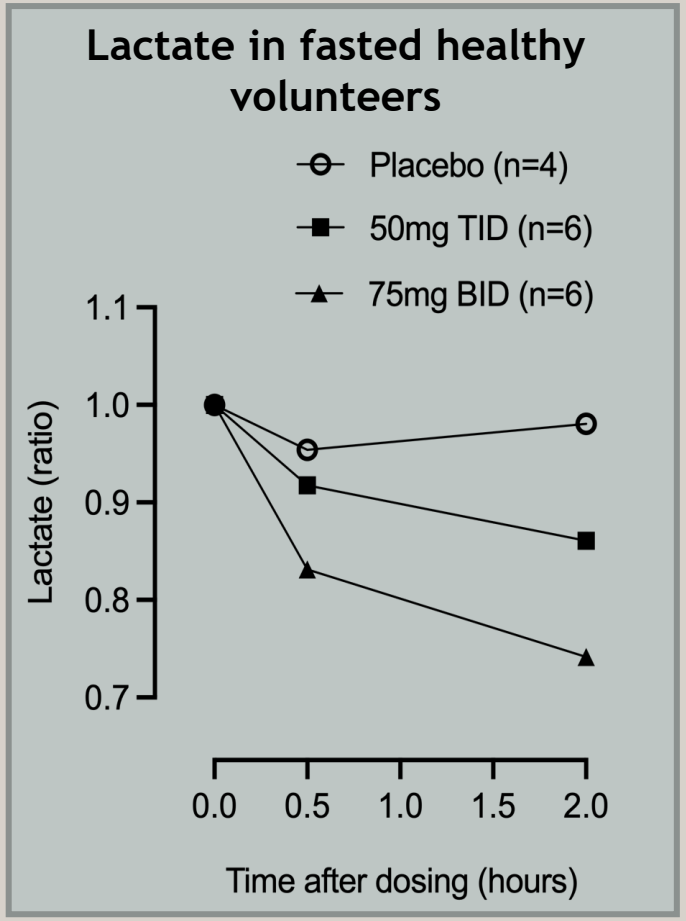
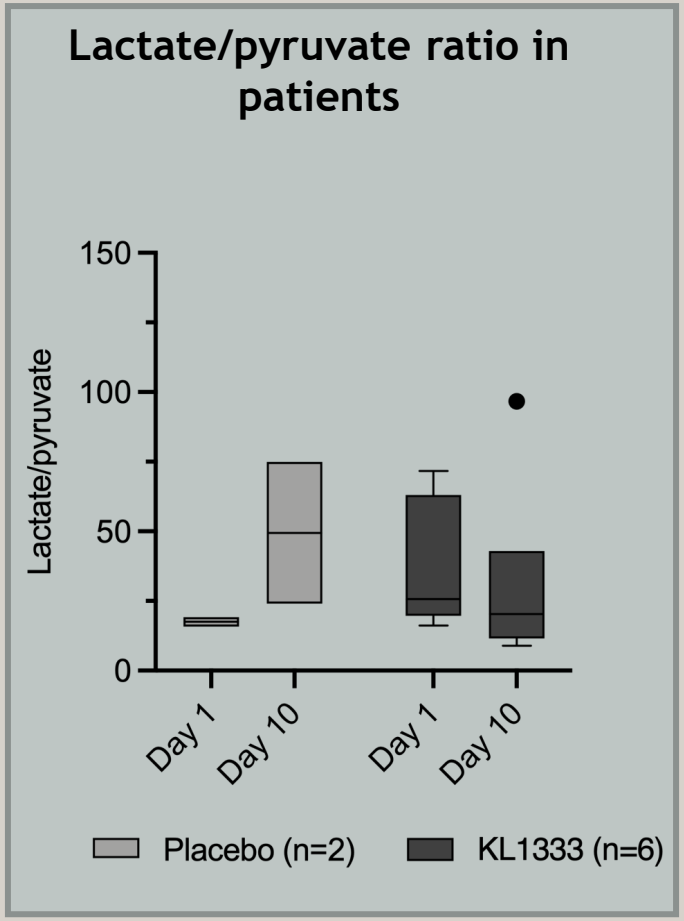
Target engagement was confirmed with lactate/pyruvate biomarker





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What is the impact of this data on the KL1333 program?

- Provides the **first evidence of efficacy of KL1333** in PMD patients
  - **Clinically-relevant endpoints** that are used in the global, registrational Phase 2 study
  - **Further strengthens the use of fatigue as an endpoint**
- Supports the **inclusion of 30 sec Sit to Stand** (measure of muscle weakness and endurance)
- **Confirmed target engagement using lactate/pyruvate**
- This study, in addition to the drug-drug interaction study that just read out, confirm a **good safety profile** for KL1333 with main dose-limiting tolerability of gastrointestinal side effects

The placebo-controlled nature of the cohort, the strong signal over a small number of patients and the association between exposure and effect give us confidence moving into the Phase 2 study.

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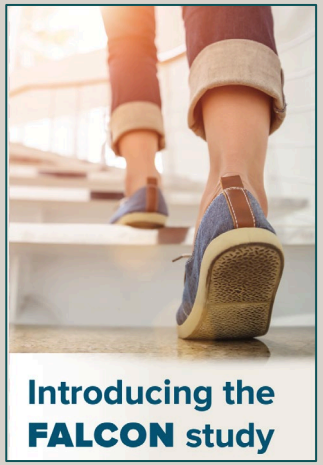
The Phase 2 FALCON study commenced in December 2022



8-12 weeks	48 weeks	5 weeks
Screening	Treatment (tablets twice daily) 40% placebo - 60% active	Follow-up

- **Design:** Randomized, double-blind, parallel-group, placebo-controlled
- **Patients:** Adult Primary Mitochondrial Disease (PMD) patients with:
  - Multisystemic mitochondrial DNA-related disease (according to category 6* of the International Classification of Inborn Metabolic Disorders)
  - Disease expressions involving at least chronic fatigue and mitochondrial myopathy/exercise intolerance
- **Treatment:** Oral twice daily dosing for 12 months (including dose titration phase)
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*Including MIDD-MELAS-m.3243A>G associated spectrum disease, single large scale mtDNA deletion associated KSS-CPEO spectrum disorders, MERRF, and other multisystemic mitochondrial DNA-related disease.; ** Newcastle Mitochondrial Disease Adult Scale (NMDAS) (Schaefer et al., 2006)

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CMC Highlights

- Drug Substance
  - Produced in Europe
  - 8-10kg GMP batch released 2020-2022
  - 36 mo stability established; 48 mo planned
  - Vendor selected for commercial scale-up

- Drug Product
  - Produced in Europe
  - Immediate release tablets in 25 mg strength
  - 36 mo stability ongoing
  - Vendor selected for commercial scale-up

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NV354

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NV354 targets high unmet need in Leigh syndrome

- Leigh syndrome is a devastating PMD with severe multiorgan deterioration and a life expectancy <five years
- 25:1,000,000 live births
- Aim to develop an energy replacement that modifies disease progression
- The indication could be expanded to other PMDs (MELAS, LHON)

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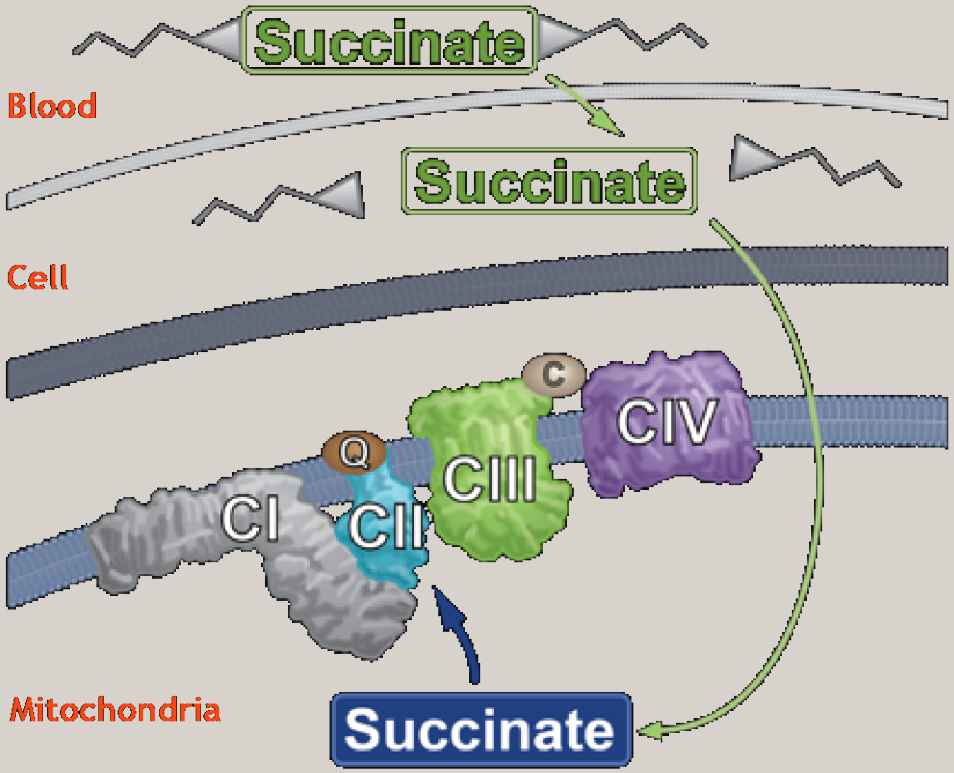
Succinate pro-drug bypasses defective Complex I



- Complex I dysfunction is one of the most common causes of mitochondrial disease
  - Key factor in Leigh Syndrome, MELAS, and LHON
- Disease modifying potential
  - Protects mitochondria and loss of organ function
  - Prevents complications caused by acute energy crisis
- Succinate pro-drug is protected by a strong patent estate and Orphan Drug Designation (US)

Ehinger et al. Nature Communications, 7:12317, August 2016

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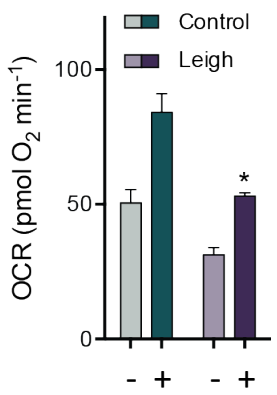
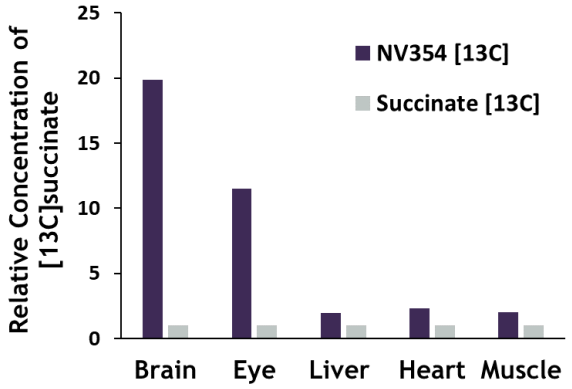
NV354 corrects underlying biochemical dysfunction in Leigh patient cells



Improved mitochondrial function in Leigh patient cells with succinate prodrug



^{13}C-labelled succinate delivery to organs

- NV354 has optimized drug properties
  - High oral bioavailability
  - High brain distribution
  - Good tolerability in toxicology studies
- Bypasses most common mutations in Leigh syndrome (complex I)
- Normalizes function of mitochondria in cells from Leigh patients

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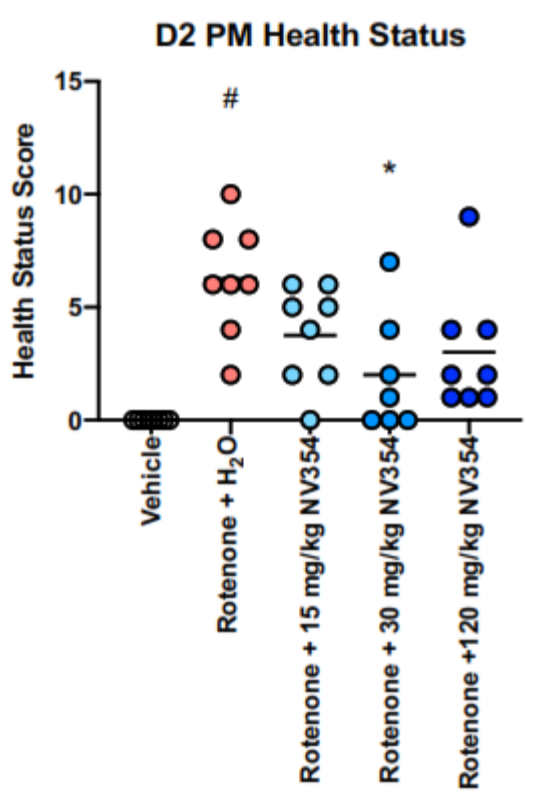
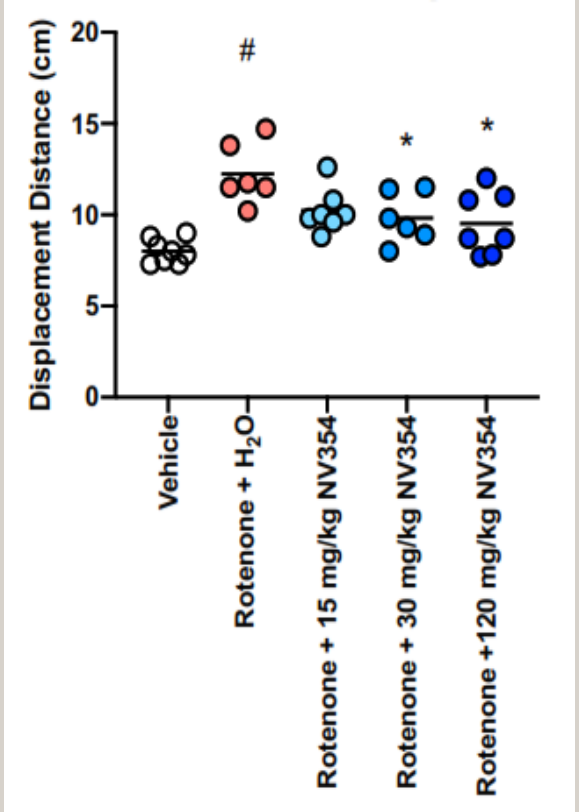
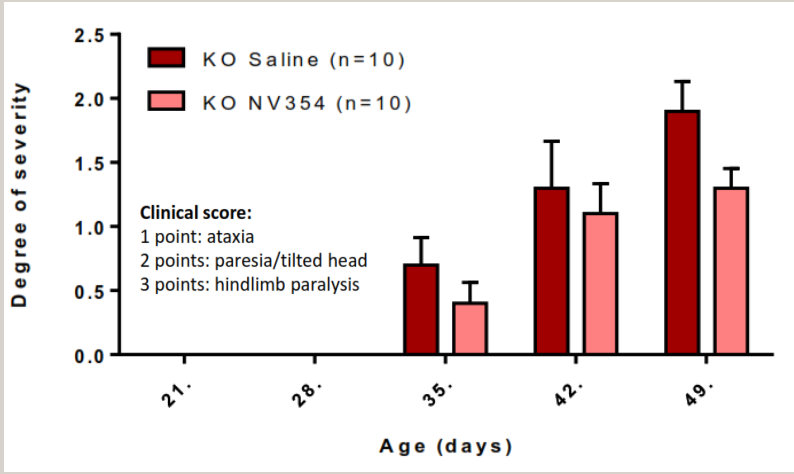
…and demonstrates efficacy in preclinical models

Toxin-induced complex I dysfunction in Rat





Genetic mouse model (Ndufs4) complex I dysfunction



- Strong early signs of preclinical efficacy in rat toxin and mouse genetic models of Leigh's Syndrome

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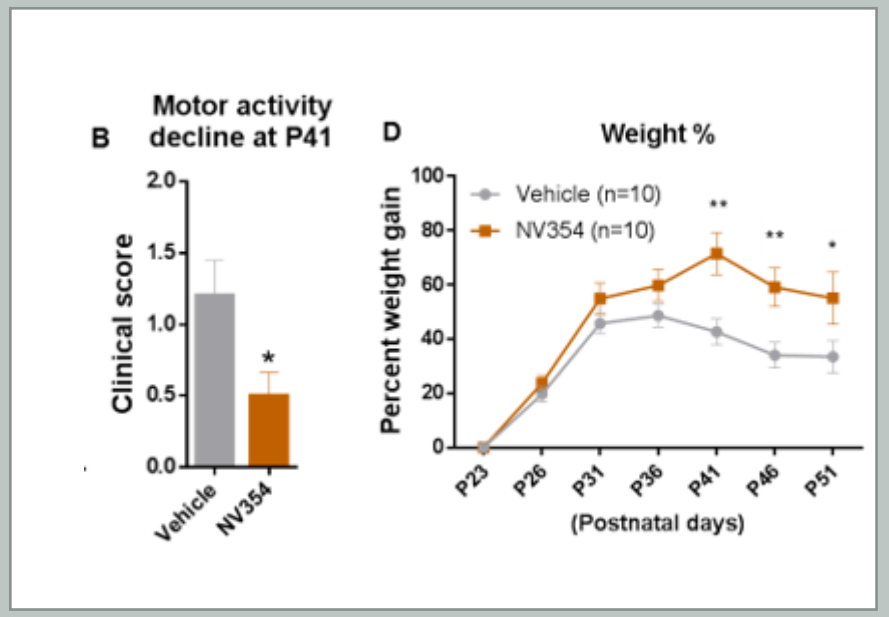
Recent data suggests impact on brain inflammation, motor activity and weight

Ndufs4 model with complex I dysfunction



UAB (Barcelona) Study with Dr. Quintana

- Decrease in neuroinflammation in brain
- Delay in the presence of clinical/motor signs
- Improved weight gain

Unpublished data; Administration of NV354 or vehicle via osmotic minipump at 70 mg/kg

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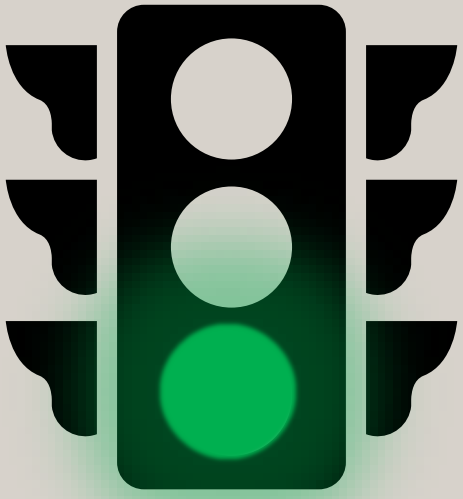
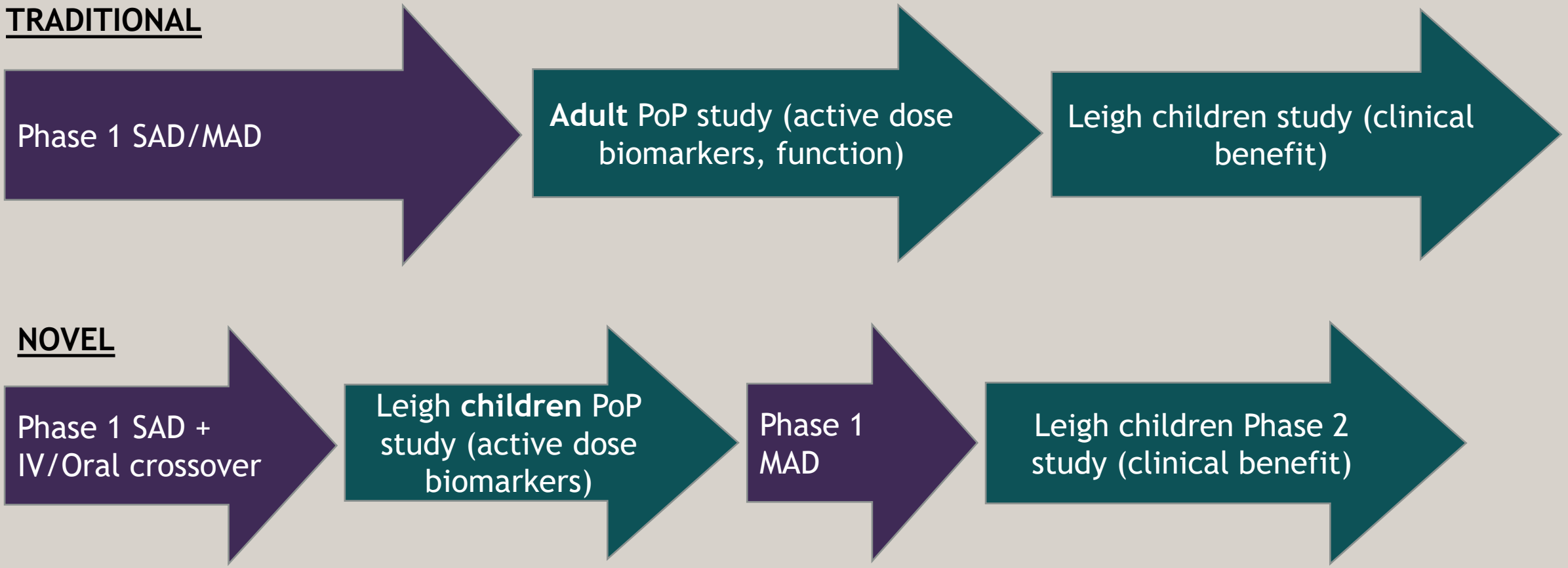
Preclinical data was discussed with UK regulators at scientific advice in late 2021…



…And they agreed that the nonclinical data package supported initiation of Phase 1 study

Novel development options being considered to shorten time and cost to patient data



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First-in-class NV354 is ready for Phase 1

In summary, NV354:

- Targets high unmet need in Leigh syndrome with expansion opportunities in other PMD indications
- Is a succinate prodrug that corrects underlying biochemical dysfunction in Leigh patient cells.
- Orally bioavailable, penetrates the brain and shows good tolerability in nonclinical species.
- Demonstrated efficient delivery of succinate to organs after i.p. or oral administration in mice.
- Efficacious in toxin-induced complex I dysfunction in Rat and genetic PMD model in mice.
- Phase 1-ready as confirmed by MHRA scientific advice meeting

Abliva is focused on becoming a global leader in mitochondrial medicine

Experienced team with 20+ years in mitochondrial research and drug development

- Offices in Lund (Sweden) and Boston (US)

Full **R&D capabilities** with a plan to **build to commercialize lead asset**

Portfolio of first-in-class clinical assets to treat **Primary Mitochondrial Diseases (PMD)**

- Phase 2 registrational study ongoing with KL1333
- NV354 is ready for Phase 1

Publicly traded on NASDAQ Sweden (ABLI, small cap)

- SEK200M (approx. $20M) raise completed in June 2022

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