Focused on Improving the Lives of Patients with Rare Genetic Mitochondrial Diseases

Moving Mito Medic[illegible]:
Reneo STRIDE St[illegible]

Reneo Overview

Our mission is to address the major challenges of patients with genetic metabolic myopathies by improving their endurance, fatigue and overall well-being

How are we moving medicines to move you?

- Using FDA's regulatory tools to aid drug development.

REN001/Primary Mitochondrial Myopathy:

- "Orphan" designation
- "Fast track" status

Orphan designation sought and granted

Reneo context:

- *Drugs… for the prevention, diagnosis, or treatment of diseases or conditions affecting **fewer than 200,000** persons in the US*

- FDA- Orphan designation granted 2020 for "***treatment of primary mitochondrial myopathy***"

  - *Designation intended to encourage companies to develop drugs to treat rare diseases*
  - *Sponsor needs to provide an annual **progress report** to FDA*

FDA "Fast Track" designation sought and granted

FDA Toolkit of expedited programs for serious conditions- drugs and biologicals

- Fast track designation √
- *Breakthrough designation*
- *Accelerated approval*
- *Priority Review designation*

Fast track designation (1)

Qualifying criteria:

- A drug that is intended to treat a serious condition **AND** nonclinical or clinical data demonstrate the potential to address unmet medical need

OR

- A drug that has been designated as a qualified infectious disease product

Fast Track designation (2)

- Benefits:
  - FDA actions to expedite development and review
  - FDA 'rolling review'
- Beware:
  - Designation may be rescinded if it no longer meets the qualifying criteria for fast track

Recent ‘fast track’ successes for patients

- 35 drugs approved via FDA fast track in 2020.

Examples:

- Margetuximab-CMKB for metastatic breast cancer
- Risdiplam for spinal muscular atrophy
- Remdesivir for Covid-19 infection
- Dojolvi as a source of calories and fatty acids for LC-FAOD

“Breakthrough” designation

- A drug that is intended to treat a serious condition AND preliminary clinical evidence indicates that the drug may demonstrate substantial improvement on a clinically significant endpoint(s) over available therapies

Recent examples:

- In 2020, 15/23 were cancer treatments

“Accelerated approval”

- A drug that treats a serious condition AND generally provides a meaningful advantage over available therapies AND demonstrates an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality (IMM) that is reasonably likely to predict an effect on IMM or other clinical benefit (i.e., an intermediate clinical endpoint)

- Examples: 12/52 newly approved drugs in 2020 used this route. Often cancer drugs.

"Priority Review"

- An application (original or efficacy supplement) for a drug that treats a serious condition AND, if approved, would provide a significant improvement in safety or effectiveness

  (Abbreviated scope-additional categories not listed here)

- Examples: 30/53 new drugs given priority review in 2020- often cancer drugs

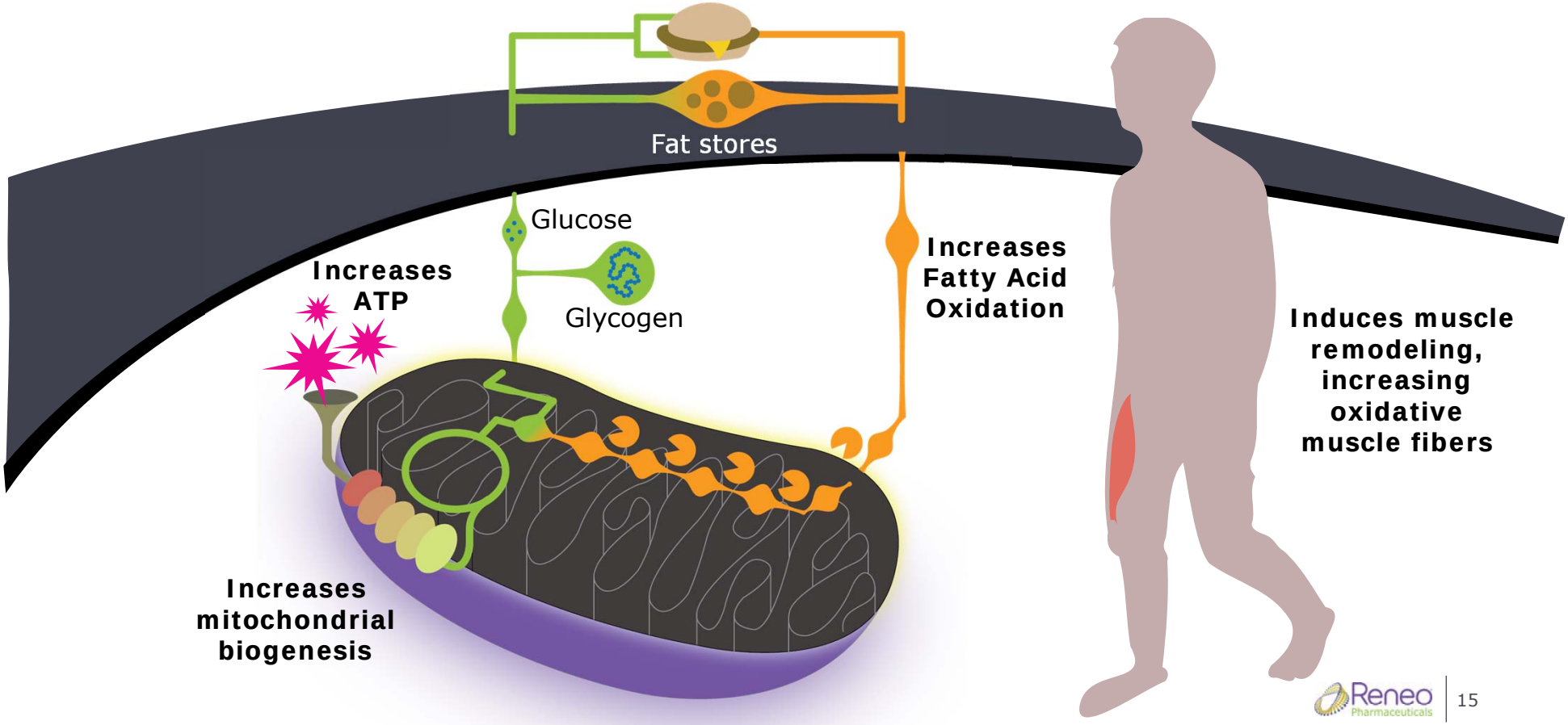
- Note more than one regulatory tool may have been used.

- Data source: https://www.fda.gov/drugs/new-drugs-fda-cders-new-molecular-entities-and-new-therapeutic-biological-products/new-drug-therapy-approvals-2020#accelerated-approval

- *Questions?*

REN001- Why Pri[illegible]y Mitochondrial Myo[illegible]y?

REN001 is an Oral PPARδ Agonist

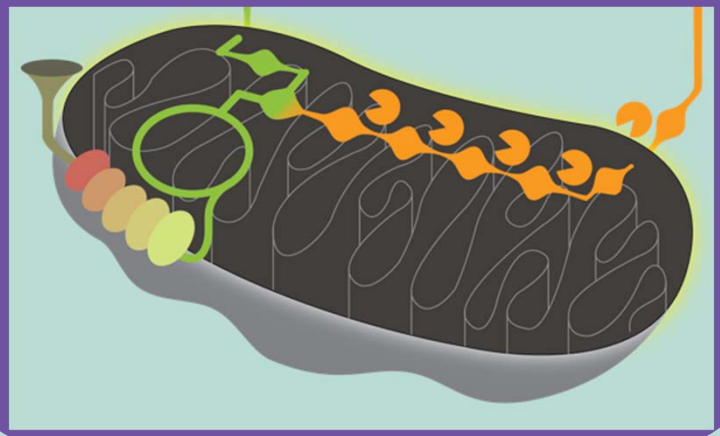


Primary Mitochondrial Myopathies

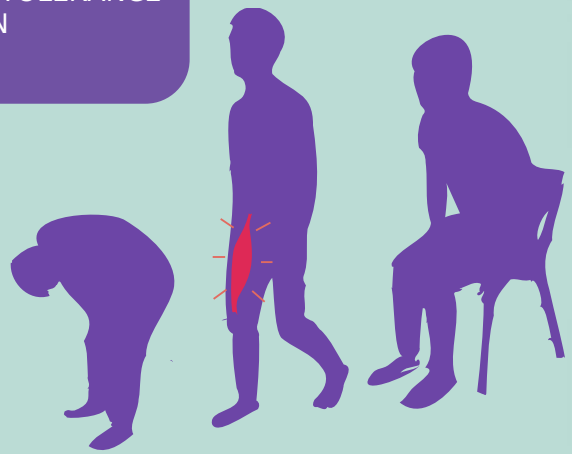
PREVALENCE
~40,000 US
~40,000 EU

TREATMENT
NO APPROVED DRUGS
VITAMINS & SUPPLEMENTS

CAUSE
MUTATIONS IN mtDNA AND nDNA
ENCODING MITOCHONDRIAL PROTEINS



SYMPTOMS
MYOPATHY
LACK OF ENDURANCE
EXERCISE INTOLERANCE
MUSCLE PAIN
FATIGUE



Rationale

- "Red thread" running from bench to animal model to healthy volunteers to a very small open-label patient study.
  - *Animal models*
  - *Healthy volunteers*
  - *Open-label patient study: improvements in endurance and how patients felt*

- So, this information allowed us to apply for orphan and fast track designations

What's next?

Study Update
REN001-201: The “STR[illegible]dy

Disclosures

- This study is funded by Reneo Pharma Ltd
- REN001 is an investigational drug and is not available outside our research program
- The safety and efficacy of REN001 has not yet been established
- It is therefore as yet unknown whether REN001 will receive regulatory approval for prescription to patients in routine medical care
- The information provided is available on the public register, clinicaltrials.gov

Stride Study

- Full title: "*A double-blind, placebo-controlled, study to evaluate the efficacy and safety of 24 weeks treatment with REN001 in patients with primary mitochondrial myopathy (PMM)*"

- ClinicalTrials.gov Identifier: NCT04535609

- Available at: https://www.clinicaltrials.gov/ct2/show/NCT04535609

Stride Study

- Adult male and female subjects (18+ years)
  - *with PMM as defined by the International Workshop:*

  "Outcome measures and clinical trial readiness in primary mitochondrial myopathies in children and adult" (Mancuso et al 2017).

- With defined mitochondrial DNA mutations only
- PMM characterized by exercise intolerance or active muscle pain
- Able to perform a walking test independently
- Women who could get pregnant are eligible provided they use highly effective contraception

Stride Study

Design

- Multicentre, multinational, double-blind, placebo-controlled parallel groups
- Placebo vs 100 mg REN001 (1:1 ratio)
- 24 weeks of once daily dosing with food

Subjects

- Adult male and female subjects (18+ years) with PMM
- With defined mitochondrial DNA mutations only
- PMM characterized by exercise intolerance or active muscle pain
- Able to perform a walking test independently
- Women who could get pregnant are eligible provided they use highly effective contraception

Outcome Measures

Primary Endpoint at Wk 24

- Change distance walked

Secondary Endpoints at Wk 24

- Change MFIS physical sub-score
- PGIC – muscle symptoms

Safety & PK Endpoints

Exploratory Endpoints

- Functional
- Quality of Life

For more information

- ClinicalTrials.gov

https://www.clinicaltrials.gov/ct2/show/NCT04535609

- MitoAction

https://www.mitoaction.org/clinicaltrials/current-clinical-trials/

- *Questions?*

Thank You!