ISRCTN92370847 https://doi.org/10.1186/ISRCTN92370847

Trial to evaluate the efficacy and safety of daily subcutaneous injections of elamipretide in subjects with primary mitochondrial disease resulting from pathogenic nuclear DNA mutations (nPMD)

Submission date
12/02/2022

Recruitment status
No longer recruiting

Registration date
06/05/2022

Overall study status
Completed

Last Edited
18/12/2025

Condition category
Genetic Diseases

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
Mitochondrial diseases are long-term genetic disorders that occur when the mitochondria (the powerhouses of the cell) fail to produce enough energy for the body to function properly. Stealth BioTherapeutics Inc. has begun a study of an investigational drug called elamipretide as a possible treatment for nuclear DNA primary mitochondrial disease (nPMD). Elamipretide is a molecule that targets the inner lining (membrane) of mitochondria where energy production occurs and normalises its structure and function, leading to an overall improvement in the function of the cell and organ. The main aim of this study is to learn how well the study drug works and how safe the study drug is compared with placebo. A placebo is an inactive material that looks like the study drug but does not have any active study drug within it.

Who can participate?
Patients aged between 18 and 70 years with nPMD

What does the study involve?
Participants are randomly allocated to take either 60 mg of elamipretide or placebo (dummy drug) by daily injection for 48 weeks. They will return to the clinical site for the week 12, 24, 36, and 48 visits for assessments, to administer the study drug, and to return all used study drug supplies. At the week 48 visit, the subjects will be administered the study drug and will enter into the 4-week follow-up period concluded by the week 52 end-of-trial visit.

What are the possible benefits and risks of participating?
Taking blood samples may cause discomfort, swelling, pain, redness, bruising, bleeding, or infection (infection rarely happens) at the site where the needle is inserted, a feeling of light-headedness when the blood is taken, and rarely fainting. Skin irritation is rare but could occur during an ECG from the electrode patches/sensors or gel that is used. Besides injection site

reactions, other side effects reported in participants dosed with elamipretide in a similar manner to this study (subcutaneous and for longer than a week) were upper respiratory tract infections, dizziness, headache, nausea and fatigue.

Where is the study run from?
Stealth BioTherapeutics Inc. (USA)

When is the study starting and how long is it expected to run for?
August 2021 to April 2024

Who is funding the study?
Stealth BioTherapeutics Inc. (USA)

Who is the main contact?
Rekha Sathyanarayana
rekha.sathyanarayana@stealthbt.com

Contact information

Type(s)
Scientific

Contact name
Mr Jim Carr

Contact details
Chief Clinical Development Officer
140 Kendrick Street, Building C-West
Needham
United States of America
MA 02494
+1 (0)617 762 2503
Jim.Carr@StealthBT.com

Type(s)
Principal investigator

Contact name
Dr Gráinne Gorman

Contact details
Freeman Road
High Heaton
Newcastle upon Tyne
United Kingdom
NE7 7DN
+44 (0)191 208 8326
grainne.gorman@newcastle.ac.uk

Type(s)
Public

Contact name
Ms Rekha Sathyanarayana

Contact details
140 Kendrick Street
Building C-West
Needham
United States of America
MA 02494
+1 (0)617 762 2579
rekha.sathyanarayana@stealthbt.com

Additional identifiers

Clinical Trials Information System (CTIS)
2021-003907-16

Integrated Research Application System (IRAS)
1004666

ClinicalTrials.gov (NCT)
NCT05162768

Protocol serial number
SPIMD-301, IRAS 1004666, CPMS 51236

Study information

Scientific Title
A Phase III randomized, double-blind, parallel-group, placebo-controlled trial to evaluate the efficacy and safety of daily subcutaneous injections of elamipretide in subjects with primary mitochondrial disease resulting from pathogenic nuclear DNA mutations (nPMD)

Study objectives
1. To evaluate the effect of single daily subcutaneous (SC) administration of elamipretide for 48 weeks on the distance walked (in meters) on the 6-Minute Walk Test (6MWT)
2. To evaluate the effect of single daily SC administration of elamipretide for 48 weeks as measured by changes in the:
2.1. Total time (in seconds) the Five-Times Sit-to-Stand Test (5XSST)
2.2. Total time (in seconds) the Triple Timed Up-and-Go Test (3TUG)
2.3. Patient Global Impression (PGI) of Change Scale
3. To evaluate the safety and tolerability of single daily SC doses of elamipretide administered for 48 weeks

Ethics approval required
Old ethics approval format

Ethics approval(s)

Approved 10/02/2022, East Midlands - Leicester Central Research Ethics Committee (Equinox House City Link, Nottingham, NG2 4LA, UK; +44 (0)2071048181; leicestercentral.rec@hra.nhs.uk), ref: 22/EM/0058

Study design
Randomized placebo-controlled double-blind parallel-group trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Primary mitochondrial disease resulting from pathogenic nuclear DNA mutations (nPMD)

Interventions
This randomized, double-blind, parallel-group, placebo-controlled trial will enrol approximately 130 subjects, consisting of 90 subjects who have nPMD with nuclear DNA (nDNA) mutations of the mitochondrial replisome for primary analysis, and an additional subset of up to 40 subjects who have nPMD with other nDNA mutations.

1. 48 weeks of single daily SC doses of 60 mg elamipretide
2. 48 weeks of single daily SC doses of placebo

The randomization will be based on a 1:1 ratio of elamipretide to matching placebo. The randomization will be centrally administered through an Interactive Web Response Systems (IWRS). Subjects will be stratified by the subclassification of the mutation type involved in the presentation of nPMD: either (1) replisome-related mutation or (2) other pathogenic mutation specific to nDNA.

The subject will return to the clinical site for the Week 12, Week 24, Week 36, and Week 48 Visits for assessments, to administer the IMP, and to return all used IMP supplies. At the Week 48 Visit, the subjects will be administered IMP and will enter into the 4-week follow-up period concluded by the Week 52 End-of-Trial Visit.

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
Elamipretide

Primary outcome(s)
Distance walked (in meters) on the 6MWT measured at baseline, Weeks 12, 24, 36, 48 and 52 (End of Trial Visit)

Key secondary outcome(s))

1. Total time (in seconds) on the Five Times Sit-to-Stand Test (5XSST) at baseline, Weeks 12, 24, 36, 48, 52 (End of Trial Visit)
2. Total time (in seconds) on the Triple Timed Up-and-Go Test (3TUG) at baseline, Weeks 12, 24, 36, 48, 52 (End of Trial Visit)
3. Patient-reported current health status measured using the Patient Global Impression of Change (PGI) of Change Scale at baseline, Weeks 12, 24, 36, 48, 52 (End of Trial Visit)

Completion date
11/04/2024

Eligibility

Key inclusion criteria
1. Willing and able to provide a signed informed consent form (ICF) prior to participation in any trial-related procedures
2. Agrees and is able to adhere to the trial requirements for the length of the trial, including administration of assigned treatment
3. ≥18 years and ≤70 years of age at the time of screening
4. Diagnosed with nPMD with a predominant clinical manifestation of myopathy, which must include progressive external ophthalmoplegia (PEO) and exercise intolerance and/or skeletal muscle weakness, with genetic confirmation of either:
4.1. Nuclear DNA mutation of the mitochondrial replisome (replisome related mutations), which include the following genes: POLG 1/2, TWINKLE (C10ORF2), TYMP, DGUOK, TK2, RRM2B, RNASEH1, SSBP, MGME1, DNA2, ANT1 (SLC25A4), SUCLG1, SUCLA2, MPV17
4.2. Other pathogenic mutations specific to nuclear DNA
5. Women of childbearing potential must agree to use one of the following methods of birth control from the date they sign the ICF until 28 days after the last dose of IMP:
5.1. Abstinence, when it is in line with the preferred and usual lifestyle of the subject. Subject agrees to use a highly effective method of contraception should they become sexually active
5.2. Relationships with male partners who have been surgically sterilized by vasectomy (the vasectomy procedure must have been conducted at least 60 days prior to the Screening Visit)
5.3. Barrier method (e.g., condom or occlusive cap) with spermicidal foam/gel/film/cream AND either hormonal contraception (oral, implanted, or injectable) or an intrauterine device or system
Note: Non-childbearing potential is defined as surgical sterilization (e.g., bilateral oophorectomy, hysterectomy, or tubal ligation) or postmenopausal (defined as permanent cessation of menstruation for at least 12 consecutive months prior to the Screening Visit)
6. Male subjects with female partners of childbearing potential must be willing to use a highly effective method of contraception from the date they sign the ICF until 28 days after the last dose of IMP

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 years

Upper age limit
70 years

Sex
All

Total final enrolment
102

Key exclusion criteria
1. Subject is unable to perform the 6MWT, 3TUG, or 5XSST functional tests. The use of a gait assist device is allowed; however, use should remain consistent for the entire duration of the trial.
2. Female subjects who are pregnant, planning to become pregnant, or breastfeeding/lactating
3. Walks <200 m or >450 m during the 6MWT (Screening visit only)
4. The estimated glomerular filtration rate (eGFR) is <30 ml/min/1.73 m² using the Modification of Diet in Renal Disease (MDRD) Study equation (Screening visit only)
5. Subject has undergone an in-patient hospitalization within 30 days prior to screening or has a planned hospitalization or a surgical procedure during the trial, unless in the opinion of the Investigator it is concluded that it will not impact the outcome measurements of the trial
6. Subject has clinically significant respiratory disease and/or cardiac disease that would interfere with trial assessments, in the opinion of the Investigator
7. Subject has had any prior interventional cardiac procedure (e.g., cardiac catheterization, angioplasty/percutaneous coronary intervention, balloon valvuloplasty, etc) within 3 months prior to screening
8. Subject has a history of or current severe neurologic impairment, severe epilepsy, severe ataxia, or severe neuropathy that may interfere with their ability to complete all trial requirements, in the opinion of the Investigator
9. Active malignancy or any other cancer from which the subject has been disease-free for <2 years. Localized squamous or non-invasive basal cell skin carcinomas are allowed, if appropriately treated prior to screening.
10. Subject has had a solid organ transplant
11. Subject has been previously diagnosed with human immunodeficiency virus (HIV), hepatitis B, or hepatitis C infection
12. Subject has a history of a systemic eosinophilic illness and/or an eosinophil count >1,000 cells x10e6/l at the Screening Visit
13. Subject is currently participating or has participated in an interventional clinical trial (i.e., investigational product or device, stem cell therapy, gene therapy) within 30 days prior to current trial; or is currently enrolled in a non-interventional clinical trial that, in the opinion of the Investigator, may be potentially confounding to the results of the current trial (e.g., exercise therapy trial).
14. Subject has received elamipretide (MTP-131) within the past one year of the Screening Visit
15. Subject has a history of active substance abuse during the year prior, in the opinion of the Investigator
16. Subject has any prior or current medical condition that, in the judgment of the Investigator, would prevent the subject from safely participating in and/or completing all trial assessments and requirements to the best of their ability

Date of first enrolment
29/04/2022

Date of final enrolment
05/10/2023

Locations

Countries of recruitment
United Kingdom

England

Australia

Germany

Hungary

Italy

Netherlands

Norway

Spain

Study participating centre
National Hospital for Neurology & Neurosurgery
Queen Square
London
England
WC1N 3BG

Study participating centre
Department of Clinical Neurosciences
University Neurology Unit
Level 5 "A" Block, Box 165
Cambridge
England
CB2 0QQ

Sponsor information

Organisation
Stealth BioTherapeutics (United States)

ROR
https://ror.org/045frfm13

Funder(s)

Funder type
Industry

Funder Name
Stealth BioTherapeutics Inc.

Results and Publications

Individual participant data (IPD) sharing plan
The pooled study datasets generated and or analyzed in this study will be included in the final study report submission and subsequent results publication. The individual de-identified participant datasets generated and/or analyzed in this study are only expected to be made available after the final study report submission upon request submitted to the Sponsor from the Clinical Investigator.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes