ISRCTN59733193 https://doi.org/10.1186/ISRCTN59733193

ReNEW: a clinical trial investigating the efficacy and safety of elamipretide in subjects who have dry age-related macular degeneration (Dry AMD)

Submission date
08/05/2024

Recruitment status
No longer recruiting

Registration date
20/08/2024

Overall study status
Ongoing

Last Edited
20/08/2024

Condition category
Eye 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
Age-related macular degeneration (AMD) is the leading cause of irreversible blindness in people aged 55 or older in the developed world. Research suggests that dry AMD is caused by damage and deterioration of the mitochondria, which are constituents of the body's cells that produce energy. Damage to the mitochondria in certain cell types within your retina (the back of your eye) may contribute to the loss of vision seen in the disease. There is currently no treatment for dry AMD. The study drug, elamipretide, is a mitochondrial protective agent that has been shown to improve cell viability and organ function across a spectrum of diseases, including ophthalmic diseases such as dry AMD. In models of dry AMD, elamipretide has been shown to improve retinal mitochondrial function, prevent disease progression, and improve visual function. The information gained in this research study will help to find out if elamipretide could be used for the treatment of dry AMD. The main aim of this study is to evaluate how safe and tolerable daily subcutaneous injections of elamipretide are.

Who can participate?
Adults who are over 55 years old and have dry AMD

What does the study involve?
Participants will receive daily subcutaneous injections of elamipretide, or placebo (randomization 2: 1) for up to 96 weeks. Participants will either inject themselves or a caregiver will administer the injections. Overall, the study will last up to 104 weeks for each participant, with 12 study visits during this period. Participants may also enter an open-label phase of the study after the 96-week treatment period. At each of the 12 study visits, participants will undergo several eye examinations, including imaging of the retina (the back of the eye), blood tests, and physical examinations, and the study doctor will do a review of their medical history, and ask about what other medications they are taking in addition to elamipretide.

About 360 patients are expected to take part in this study at approximately 65 clinical trial sites around the world. The clinical trial sites are usually specialist eye hospitals or ophthalmology clinics in general hospitals.

What are the possible benefits and risks of participating?
There is no guarantee of benefits for participants but elamipretide may help to prevent the progression of dry AMD. Participants may also experience some side effects or discomforts of taking elamipretide and may experience some side effects and discomforts associated with procedures or assessments that they undergo during study visits. The study doctor explains all possible risks of participating thoroughly to potential participants before they agree to take part.

Where is the study run from?
Stealth BioTherapeutics, Massachusetts, USA

When is the study starting and how long is it expected to run for?
May 2024 to August 2027

Who is funding the study?
Stealth BioTherapeutics, Massachusetts, USA

Who is the main contact?
Rekha Sathyanarayana (Stealth BioTherapeutics), Rekha.Sathyanarayana@stealthbt.com

Study website
https://dry-amdclinicaltrials.com/

Contact information

Type(s)
Scientific

Contact name
Mr Jim Carr

Contact details
123 Highland Avenue Suite 201
Needham
United States of America
02494
+1 617-762-2503
Jim.Carr@StealthBT.com

Type(s)
Principal Investigator

Contact name
Dr Christiana Dinah

Contact details

Acton Lane
London
United Kingdom
NW10 7NS
+44 20 84532020
christiana.dinah@nhs.net

Additional identifiers

EudraCT/CTIS number
2024-511482-11-00

IRAS number
1010005

ClinicalTrials.gov number
NCT06373731

Secondary identifying numbers
SPIAM-301, IRAS 1010005

Study information

Scientific Title
ReNEW: A phase 3, randomized, double-masked, placebo-controlled clinical trial to evaluate the efficacy, safety, and pharmacokinetics of subcutaneous injections of elamipretide in subjects who have dry age-related macular degeneration (Dry AMD)

Acronym
ReNEW

Study objectives
The main objective of the trial is to evaluate the efficacy of daily injections of elamipretide in subjects who have dry age-related macular degeneration (AMD).

The secondary objectives are as follows:
1. To evaluate how safe and tolerable the daily injections of elamipretide are for the subjects
2. To evaluate the pharmacokinetic (PK) profile of elamipretide and its metabolites. That is, how the body deals with the drug, including concentration of the drug in the blood stream, how the body breaks the drug down and how long the it takes for the body to remove the drug or its breakdown products

Ethics approval required
Ethics approval required

Ethics approval(s)
1. Approved 22/03/2024, The Advarra Center for IRB Intelligence (CIRBI) (6100 Merriweather Dr., Suite 600, Columbia, MD 21044, United States of America; +1-866-992-4724; cirbi@advarra.com), ref: None provided

2. Approved 08/05/2024, London - Riverside REC (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 2071048171; riverside.rec@hra.nhs.uk), ref: 24/LO/0418

3. Approved 30/07/2024, Northern B Health and Disability Ethics Committee (Ministry of Health Health and Disability Ethics Committees PO Box 5013, Wellington, 6140, New Zealand; -; hdecs@health.govt.nz), ref: 2024 FULL 20251

Study design
Interventional double blind randomized placebo controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Safety, Efficacy

Participant information sheet
Not available in web format, please use the contact details to request a participant information sheet

Health condition(s) or problem(s) studied
Dry age-related macular degeneration (dry AMD)

Interventions
Subjects will be randomized (2:1) to once daily 40 mg SC of elamipretide or placebo for 96 weeks of treatment, by an online central randomization system (Interactive Response Technology). Trial personnel and subjects will be masked to treatment until the database is locked at the end of the trial unless unmasking is needed in a medical emergency.

Intervention Type
Drug

Pharmaceutical study type(s)
Pharmacokinetic, Therapy

Phase
Phase III

Drug/device/biological/vaccine name(s)
Elamipretide [D-Arginyl-2’,6’-dimethyl-L-tyrosyl- L –lysyl- L –phenylalaninamide (free base)]

Primary outcome measure

The rate of change in the macular area of photoreceptor loss (defined as an Ellipsoid Zone-Retinal Pigment Epithelium thickness of 0µm) assessed by Spectral Domain-Optical Coherence Tomography and EZ mapping at Week 48

Secondary outcome measures
1. Rate of change in the macular area of photoreceptor loss (defined as an EZ-RPE thickness of 0µm) assessed by SD-OCT and EZ mapping at Week 72
2. Rate of change in the macular area of photoreceptor loss (defined as an EZ-RPE thickness of 0µm) assessed by SD-OCT and EZ mapping at Week 96
3. Proportion of subjects gaining ≥ 10 letters (2 lines) in Low Luminance Best- Corrected Visual Acuity (LL BCVA) from baseline at Week 48
4. Proportion of subjects gaining ≥ 15 letters (3 lines) in LL BCVA from baseline at Week 48

Overall study start date
30/05/2024

Completion date
01/08/2027

Eligibility

Key inclusion criteria
A subject must meet all the inclusion criteria at the Screening and Baseline Visit (unless otherwise specified) to be eligible for inclusion in the trial.

1. Adults ≥55 years of age with at least 1 eye with dry AMD with photoreceptor loss, as determined at the Screening Visit by the presence of extrafoveal Geographic Atrophy (GA), as determined by the Reading Centre primarily by Fundus Autofluorescence. For this trial, extrafoveal GA is defined as:
1.1. well-demarcated area(s) of GA
1.2. All GA lesions must be at least 150 µm from foveal center. Note: The fellow eye may have any of the following: no AMD, AMD without GA, AMD with GA, CNV AMD, or foveal GA (ongoing treatment with anti-angiogenic therapies and/or complement inhibitor therapies in the fellow eye is allowable)

Ocular conditions – Study Eye:
2. GA in the study eye at the Screening Visit may be multi-focal, but the cumulative GA lesion and size (by FAF, as determined by the Reading Centre) must:
2.1. Be ≥0.50 mm^2 and ≤10.16 mm^2 AND
2.2. Reside completely within the FAF 30- or 35-degree image
3. Best corrected visual acuity (BCVA) by Early Treatment Diabetic Retinopathy Study (ETDRS) score of ≥55 letters in the study eye
4. Low Luminance BCVA by ETDRS score of ≥ 10 letters in the study eye
5. LLD (defined as the difference between BCVA and LL BCVA) of >5 letters in the study eye
6. Sufficiently clear ocular media, adequate pupillary dilation, fixation to permit quality fundus imaging, and ability to cooperate sufficiently for adequate ophthalmic visual function testing and anatomic assessment in the study eye
7. Able to administer Investigational Medicinal Product (IMP) or have an appropriate designee who can administer the IMP (i.e., a capable family member or caregiver)
8. Able to provide informed consent and willing to comply with all site visits, examinations, daily

IMP administrations, dosing diary entries and other conditions of the trial protocol
9. Women of childbearing potential must agree to use 1 of the following methods of contraception from the date they sign the ICF until 28 days after the last dose of IMP:
9.1. 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
9.2. Relationships with male partners who have been surgically sterilized by vasectomy (the vasectomy procedure must have been conducted at least 60 days before the Screening Visit)
9.3. 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 before the Screening Visit)
10. Male subjects with female partners of childbearing potential must be willing to use a highly effective method of contraception (e.g., abstinence, dual method of contraception) from the date they sign the ICF until 28 days after the last dose of IMP

Participant type(s)
Patient

Age group
Adult

Lower age limit
55 Years

Sex
Both

Target number of participants
360

Key exclusion criteria
Subjects who meet any of the following criteria at the Screening and Baseline Visit (unless otherwise specified) will be excluded from the trial:
1. The absence of observable hyper-FAF at the margins of the GA in the study eye at the Screening Visit by the Reading Centre
2. Atrophic retinal disease of causality other than AMD including myopia-related maculopathy and monogenetic macular dystrophies including pattern dystrophy and adult-onset Stargardt disease in the study eye
3. Evidence of exudative AMD or choroidal neovascularisation (CNV) by history or fluorescein angiography (FA) in the study eye, as determined by the Reading Centre
4. Presence of retinal vein occlusion in the study eye
5. Presence of vitreous haemorrhage in the study eye
6. History of retinal detachment in the study eye
7. History of macular hole (stages 2 to 4) in the study eye
8. Presence of an epiretinal membrane and/or vitreomacular traction in the study eye that causes distortion of the retinal contour
9. Presence of any retinal pathology in the study eye that prohibits outer retinal quantification and ellipsoid zone (EZ) mapping, as determined at the Screening Visit by the Reading Centre
10. At the Screening Visit, advanced glaucoma resulting in a cup to disc ratio of > 0.8 in the study eye

11. History of glaucoma filtration surgery or uncontrolled glaucoma at Baseline Visit in the opinion of the Investigator OR currently using > 2 medications (minimally invasive glaucoma surgeries (e.g., MIGS) are allowable). Note: Combination medications count as 2 medications.
12. Presence of visually significant cataract OR presence of significant posterior capsular opacity in the setting of pseudophakia. Note: Significant cataract is defined as > +2 nuclear sclerosis based upon the scale below or any Posterior Subcapsular Cataract in the study eye. The Sponsor, or its designee, will supply the clinical trial sites with a copy of the standard photographs. Grade descriptions:
Grade 1: Opacity is present
Grade 2: Opacity is present, but less than Nuclear Standard Photograph #2
Grade 3: Opacity is present, and as severe as or worse than Nuclear Standard Photograph #2.
Source: (Chew 2010).
13. Presence of significant keratopathy or any other media or corneal opacity that would cause scattering of light or alter visual function, especially in LL conditions in the study eye
14. Ocular incisional or laser surgery (including cataract surgery) in the study eye within 90 days before the Baseline Visit
15. YAG laser capsulotomy in the study eye within 30 days before the Baseline Visit
16. Aphakia in the study eye
17. History of vitrectomy surgery, submacular surgery, or any vitreoretinal surgery in the study eye
18. Prior treatment with Visudyne® (verteporfin) ocular photodynamic therapy, external-beam radiation therapy (for intraocular conditions), or transpupillary thermotherapy in the study eye
19. History of subthreshold laser treatment or other forms of photobiomodulation for AMD in the study eye
20. Intravitreal drug delivery in the past 60 days or 5-half-lives from the Baseline Visit of the injected drug whichever is longer (e.g., intravitreal corticosteroid injection, anti-angiogenic drugs, or device implantation) in the study eye
21. Intravitreal drug delivery of a complement inhibitor in the past 6 months from the Baseline Visit in the study eye
22. Concurrent disease in the study eye that could require medical or surgical intervention during the trial
23. Presence of diabetic retinopathy (a history of diabetes mellitus without retinopathy is not a criterion for exclusion) in either eye
24. History of herpetic infection in either eye
25. Active uveitis and/or vitritis (grade trace or above) in either eye
26. History of idiopathic or autoimmune-associated uveitis in either eye
27. Active infectious conjunctivitis, keratitis, scleritis, or endophthalmitis in either eye

Systemic Conditions:
28. Has a history of a systemic eosinophilic illness and/or an eosinophil count >1,000 cells x106/L at the Screening Visit
29. History of solid organ transplant
30. Any disease or medical condition that in the opinion of the Investigator would prevent the subject from successfully participating in the trial or might confound trial results
31. Current use of medications known to be toxic to the lens, retina, or optic nerve (e.g., deferoxamine, chloroquine/hydroxychloroquine [Plaquenil®], tamoxifen, phenothiazines, ethambutol, digoxin, and aminoglycosides)
32. eGFR of < 30 mL/min at the Screening Visit (using the CKD-EPI 2021 formula)

General Conditions:
33. Participation in other investigational drug or device clinical trials within 30 days or 5 half-lives (whichever is longer) of Screening; 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
34. Women who are pregnant, planning to become pregnant, or breastfeeding/lactating
35. History of allergy to fluorescein that is not amenable to treatment
36. Inability to comply with trial or follow-up procedures
37. Inability to obtain Colour funds photography (CFP), FAF, and FA of sufficient quality to be analyzed and interpreted
38. Active malignancy or any other cancer from which the subject has been cancer-free for < 2 years. Localized squamous or non-invasive basal cell skin carcinomas are allowed, if appropriately treated prior to screening
39. History of allergic reaction to the investigational drug or any of its components
40. Prior participation in any elamipretide trial

Date of first enrolment
30/05/2024

Date of final enrolment
30/05/2025

Locations

Countries of recruitment
Czech Republic

Germany

Hungary

Italy

New Zealand

Spain

United Kingdom

United States of America

Study participating centre
-
United Kingdom
-

Sponsor information

Organisation

Stealth BioTherapeutics (United States)

Sponsor details
123 Highland Avenue, Suite 201
Needham
United States of America
02494
+161 7762 2503
Rekha.Sathyanarayana@stealthbt.com

Sponsor type
Industry

Website
https://stealthbt.com/

ROR
https://ror.org/045frfm13

Funder(s)

Funder type
Industry

Funder Name
Stealth BioTherapeutics Inc.

Results and Publications

Publication and dissemination plan
1. Publication on website
2. Submission to regulatory authorities

All information provided regarding the study, as well as all information collected/documented during the course of the study, will be regarded as confidential. The Sponsor reserves the right to release literature publications based on the Sponsor's publication policy.

Intention to publish date
29/11/2028

Individual participant data (IPD) sharing plan
The current data sharing plans for this study are unknown and will be available at a later date

IPD sharing plan summary
Data sharing statement to be made available at a later date