ISRCTN57533271 https://doi.org/10.1186/ISRCTN57533271

Mass balance study of [14C]-REN001 in healthy male subjects

Submission date 27/05/2022	**Recruitment status** No longer recruiting	[X] Prospectively registered [ ] Protocol [ ] Statistical analysis plan [ ] Results [ ] Individual participant data [ ] Record updated in last year
Registration date 01/07/2022	**Overall study status** Completed	
Last Edited 16/02/2024	**Condition category** Genetic Diseases	

Plain English summary of protocol

Background and study aims
The Sponsor is developing the test medicine, Mavodelpar (REN001), to treat three rare genetic diseases that cause muscles to not function properly. This healthy volunteer study is trying to identify how the test medicine is taken up, broken down and removed from the body. It is also looking to assess the safety and tolerability of the test medicine.

Who can participate?
Healthy male volunteers aged 30 to 65 years

What does the study involve?
The study consists of one period where six volunteers in one cohort receive a single 100 mg dose of [14C] REN001 oral solution in the fasted state (on an empty stomach) on Day 1. Volunteers' blood, urine and faeces are taken throughout the study for analysis of the test medicine and its breakdown products and of volunteer safety. Volunteers remain in the clinical unit for 14 days, however, if the relevant radioactivity criteria have not been met, volunteers may be required to remain at the clinic for a total of 16 days. If relevant criteria have not been met at this point, home collections of urine and/or faeces may be required. Volunteers are expected to be involved in this study for approximately 6 weeks, from screening to discharge.

What are the possible risks and benefits of participating?
As participants are healthy volunteers, they will get no medical benefit from taking part in this study. However, the development of a treatment for the three rare genetic diseases that cause muscles to not function properly may benefit the population as a whole. It is considered that the risk/benefit evaluation in this study supports the use of healthy volunteers. Full information on possible side effects is provided to volunteers in the Participant Information Sheet and Informed Consent Form. Volunteers are closely monitored during the study and safety assessments are performed regularly.

Where is the study run from?
Quotient Sciences Limited (UK)

When is the study starting and how long is it expected to run for?
May 2022 to October 2022

Who is funding the study?
Reneo Pharma Ltd (UK)

Who is the main contact?
recruitment@weneedyou.co.uk

Contact information

Type(s)
Principal investigator

Contact name
Dr Nand Singh

Contact details
Quotient Sciences Limited
Mere Way
Ruddington Fields
Ruddington
Nottingham
United Kingdom
NG11 6JS
+44 (0)330 303 1000
recruitment@weneedyou.co.uk

Type(s)
Scientific

Contact name
Mr Study Clinical Trial Coordinator

Contact details
[The last known address of the sponsor]
Reneo Pharma Ltd
Innovation House
Discovery Park
Ramsgate Road
Sandwich
United Kingdom
CT13 9FF

Type(s)
Public

Contact name
Mr Study Clinical Trial Coordinator

Contact details

[The last known address of the sponsor]
Reneo Pharma Ltd
Innovation House
Discovery Park
Ramsgate Road
Sandwich
United Kingdom
CT13 9FF

Additional identifiers

Clinical Trials Information System (CTIS)
2021-006892-41

Integrated Research Application System (IRAS)
1004854

Protocol serial number
Sponsor code: REN001-104, Quotient code: QSC205599

Study information

Scientific Title
An open-label, single-dose study designed to assess the mass balance recovery, metabolite profile and identification of [14C]-REN001 in healthy male subjects

Study objectives
The study is not hypothesis testing. The trial will meet the following primary and secondary objectives:

Primary objectives:
1. To determine the mass balance recovery after a single oral dose of [14C]-REN001

Secondary objectives:
1. To determine the routes and rates of elimination of [14C]-REN001
2. To perform metabolite profiling and structural identification from plasma, urine and faecal samples
3. To determine the pharmacokinetics of REN001, M351, M527 and total radioactivity in plasma
4. To evaluate the extent of distribution of total radioactivity into blood cells
5. To provide additional safety and tolerability information for REN001

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Approved 13/06/2022, Fast-Track REC (Now transferred to London - Chelsea REC) (Health Research Authority, 2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; N/A; fasttrack.rec@hra.nhs.uk), ref: 22/FT/0065
2. Approved 13/06/2022, MHRA (10 South Colonnade, Canary Wharf, London, E14 4PU, UK; +44 (0)20 3080 6000; info@mhra.gov.uk), ref: CTA 49733/0005/001-000

Primary study design
Interventional

Study design
Single-centre, open-label, non-randomized, single-period, single-dose, absorption, metabolism, distribution and elimination (ADME) study

Study type(s)
Other

Health condition(s) or problem(s) studied
Primary mitochondrial myopathy (rare genetic diseases that cause muscles to not function properly)

Interventions
Participants receive one 100 mg oral dose of [14C]-REN001 oral solution in the fasted state

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
Mavodelpar (REN001)

Primary outcome(s)
Mass balance recovery of total radioactivity in all excreta (urine and faeces): CumAe and Cum% Ae measured using liquid scintillation counting. This is assessed between Day 1 and Day 13, or later if the radioactivity criteria were not met (including additional collections in the clinical unit and/or home collections).

Key secondary outcome(s)
1. Ae, %Ae, CumAe and Cum%Ae for total radioactivity in all excreta (urine and faeces) by interval measured using liquid scintillation counting. These are assessed between Day 1 and Day 13, or later if the radioactivity criteria were not met (including additional collections in the clinical unit and/or home collections).
2. Identification of the chemical structure of each metabolite accounting for ≥10% of circulating total radioactivity (plasma) or accounting for ≥10% of the dose in urine and faeces by liquid chromatography-radio-detection with subsequent high-resolution mass spectrometry where appropriate. This is assessed between Day 1 and Day 13, or later if the radioactivity criteria were not met (including additional collections in the clinical unit and/or home collections).
3. Tlag, Tmax, Cmax, AUC(0-last), AUC(0-inf), lambda-z, T1/2, CL/F (apparent clearance), Vz/F (apparent volume of distribution), metabolite to parent ratios (based on Cmax and AUC), as applicable are measured using liquid chromatography with tandem mass spectrometry. These are assessed between Day 1 and Day 13, or later if the radioactivity criteria were not met (including additional collections in the clinical unit and/or home collections).
4. Evaluation of whole blood:plasma concentration ratios for total radioactivity for corresponding time points measured using liquid scintillation. This is assessed between Day 1 and Day 13, or later if the radioactivity criteria were not met (including additional collections in

the clinical unit and/or home collections).
5. Incidence of adverse events (AEs) collected by often asking volunteers how they are feeling and change from baseline for vital signs, electrocardiogram (ECG) parameters, and laboratory safety parameters assessed by standard Phase 1 unit monitoring. These are assessed at screening and throughout the trial.

Completion date
25/10/2022

Eligibility

Key inclusion criteria
1. Healthy males
2. Aged 30 to 65 years, inclusive, at the time of signing informed consent
3. Body mass index (BMI) of 18.0 to 30.0 kg/m2 as measured at screening
4. Must be willing and able to communicate and participate in the whole study
5. Must have regular bowel movements (i.e. average stool production of ≥1 and ≤3 stools per day)
6. Must provide written informed consent
7. Must agree to adhere to the contraception requirements defined in the clinical protocol

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
30 Years

Upper age limit
65 Years

Sex
Male

Total final enrolment
6

Key exclusion criteria
1. Subjects who have received any IMP in a clinical research study within the 90 days prior to Day 1, or within 5 elimination half-lives prior to Day 1, whichever is longer
2. Subjects who are, or are immediate family members of, a study site or sponsor employee
3. Subjects who report to have previously received REN001
4. Evidence of current SARS-CoV-2 infection
5. History of any drug or alcohol abuse in the past 2 years
6. Regular alcohol consumption in males >21 units per week (1 unit = ½ pint beer, or a 25 mL

shot of 40% spirit, 1.5 to 2 units = 125 mL glass of wine, depending on type)
7. A confirmed positive alcohol breath test at screening or admission
8. Current smokers and those who have smoked within the last 12 months. A confirmed breath carbon monoxide reading of greater than 10 ppm at screening or admission
9. Current users of e-cigarettes and nicotine replacement products and those who have used these products within the last 12 months
10. Subjects with pregnant or lactating partners
11. Radiation exposure, including that from the present study, excluding background radiation but including diagnostic x-rays and other medical exposures, exceeding 5 mSv in the last 12 months or 10 mSv in the last 5 years. No occupationally exposed worker, as defined in the Ionising Radiation Regulations 2017, shall participate in the study
12. Subjects who have been administered IMP in an ADME study in the last 12 months
13. Subjects who do not have suitable veins for multiple venepunctures/cannulation as assessed by the investigator or delegate at screening
14. Clinically significant abnormal clinical chemistry, haematology or urinalysis as judged by the investigator. Subjects with Gilbert's Syndrome are not allowed.
15. Confirmed positive drugs of abuse test result
16. Positive hepatitis B surface antigen (HBsAg), hepatitis C virus antibody (HCV Ab) or human immunodeficiency virus (HIV) 1 and 2 antibody results
17. Evidence of renal impairment at screening, as indicated by an estimated creatinine clearance (CLcr) of <80 mL/min using the Cockcroft-Gault equation
18. History of clinically significant cardiovascular, renal, hepatic, dermatological, chronic respiratory or gastrointestinal disease, neurological or psychiatric disorder, as judged by the investigator
19. Serious adverse reaction or serious hypersensitivity to any drug or the formulation excipients
20. Presence or history of clinically significant allergy requiring treatment, as judged by the investigator. Hay fever is allowed unless it is active
21. Donation of blood or plasma within the previous 3 months or loss of greater than 400 mL of blood
22. Subjects who are taking, or have taken, any prescribed or over-the-counter drug or herbal remedies (other than up to 4 g of paracetamol per day in the 14 days before IMP administration). Exceptions may apply, as determined by the investigator, if each of the following criteria are met: medication with a short half-life if the washout is such that no pharmacodynamic activity is expected by the time of dosing with IMP; and if the use of medication does not jeopardize the safety of the trial subject; and if the use of medication is not considered to interfere with the objectives of the study. COVID-19 vaccines are accepted concomitant medications.
23. Failure to satisfy the investigator of fitness to participate for any other reason

Date of first enrolment
11/09/2022

Date of final enrolment
25/10/2022

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Quotient Sciences Limited
Mere Way
Ruddington Fields
Ruddington, Nottingham
United Kingdom
NG11 6JS

Sponsor information

Organisation
Reneo Pharma Ltd

Funder(s)

Funder type
Industry

Funder Name
Reneo Pharma Ltd

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated and/or analysed during the current study will not be made available because of their high commercial sensitivity and the negligible benefit to the public of publication of results of nontherapeutic clinical trials.

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No