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A Phase I, open-label, single-dose study designed to assess the absorption, distribution, metabolism and excretion of [14C]-RLY-4008 in healthy male participants

Submission date 16/06/2022	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [_] Record updated in last year
Registration date 05/07/2022	**Overall study status** Completed	
Last Edited 18/02/2025	**Condition category** Cancer	

Plain English summary of protocol

Background and study aims
The Sponsor is developing the test medicine (RLY-4008) to treat advanced cancers. Cancer is a disease where abnormal cells in the body grow in an uncontrolled way. Advanced cancer is where the cancer has spread from the original location (metastasised) or has come back after it has been treated (recurred).
This one-part, healthy volunteer study will try to identify how the test medicine is taken up, broken down and removed from the body.

Who can participate?
This study will take place at one non-NHS site, enrolling up to 6 male volunteers aged between 30-55.

What does the study involve?
Volunteers will be given a radiolabelled version of the test medicine. 'Radiolabelled' means that the test medicine has a radioactive component which helps track where the test medicine is in the body and how it is removed. They will receive an oral capsule dose of 70 mg in the fasted state. Volunteers will be discharged between Day 15 and Day 17, radiation requirements depending.

What are the possible risks and benefits of participating?
1. As this is a Phase I study, the most relevant population is healthy volunteers. It is considered that the risk/benefit evaluation in this study supports the use of healthy volunteers.
2. There is always a risk that the stipend in healthy volunteer studies could represent coercion. The time spent in the clinic, travel, inconvenience and other expenses factor in calculating the stipend. Perception of risk is not considered in this calculation.
3. When investigating new medicines there is always a risk of unexpected side effects and occasionally allergic reactions. Volunteers will be closely monitored during the study.
4. Volunteers may experience side effects from the test medicine in this study. Full information

on possible side effects is provided to volunteers in the Participant Information Sheet and Informed Consent Form.
5. There will be an extended period of fasting for the volunteers taking part in this study. To ensure an adequate fluid intake, the volunteers will be allowed ad libitum fluids 1 hour post-dose and will be monitored for signs of dehydration and fatigue.
6. Blood samples will be collected during the study. Collection of these samples can cause soreness and bruising of the arms but these problems usually clear up within a few days to a few weeks.
7. ECG stickers on volunteers' chests and limbs may cause some local irritation and may be uncomfortable to remove but volunteers will be closely monitored to ensure any local irritation does not persist.
8. The test medicine has the potential to increase the skin's sensitivity to sunlight. Volunteers will be advised to restrict sun exposure until at least 7 days after dosing.
9. Volunteers will be exposed to 1.0 milliSieverts (mSv) of radioactivity during the study, which is equivalent to approximately 4.5 months' exposure to the average yearly background radiation in the UK (2.7 mSv). That amount of radiation poses negligible risk to the volunteers' health.
Participants will get no medical benefit from taking part in this study. We hope that the development of a product to improve the treatment of advanced cancer.

Where is the study run from?
Relay Therapeutics, Inc. (USA)

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

Who is funding the study?
Relay Therapeutics, Inc. (USA)

Who is the main contact?
Dr Chris Galloway, rly-4008-101@elevartherapeutics.com

Contact information

Type(s)
Public, Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
2022-001467-27

Integrated Research Application System (IRAS)
1005366

Protocol serial number
Study code: RLY-4008-002; Quotient code: QSC206365

Study information

Scientific Title
A Phase I, open-label, single-dose study designed to assess the absorption, distribution, metabolism and excretion of [14C]-RLY-4008 in healthy male participants

Study objectives
Primary objectives:
1. To determine the mass balance and routes and rates of excretion after a single oral dose of carbon-14 [14C]-RLY-4008
2. To perform metabolite profiling and structural identification from plasma, urine and faecal samples

Secondary objectives:
1. To identify the chemical structure of each metabolite accounting for more than 10% of circulating total radioactivity or accounting for 10% or more of the dose in excreta
2. To evaluate the extent of distribution of total radioactivity into red blood cells
3. To assess the safety and tolerability of a single oral dose of RLY-4008
4. To assess the oral pharmacokinetics (PK) of RLY-4008

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Approved 05/07/2022, Health and Social Care Research Ethics Committee B (HSC REC B) (Lissue Industrial Estate West, 5 Rathdown Walk, Lisburn, BT28 2RF, United Kingdom; +44 (0)28

9536 1406; recb@hscni.net), ref: 22/NI/0094
2. Approved 05/07/2022, MHRA (10 South Colonnade, Canary Wharf, London E14 4PU; +44 (0)20 3080 6000; info@mhra.gov.uk), ref: CTA 54249/0002/001-0001

Primary study design
Interventional

Study design
Non-randomized Phase I study to assess absorption, distribution, metabolism, and excretion in healthy volunteers

Study type(s)
Other

Health condition(s) or problem(s) studied
Cancer

Interventions
This is a non-randomised, open-label study. This healthy volunteer study will try to identify how the test medicine is taken up, broken down and removed from the body. Volunteers will be given a radiolabelled version of the test medicine. This study will take place at one non-NHS site, enrolling up to 6 male volunteers aged between 30-55. The 6 volunteers will receive an oral capsule dose of 70 mg in the fasted state. Volunteer's blood, urine and faeces will be taken throughout the study for analysis of the test medicine and for their safety. Volunteers will be discharged between Day 15 and Day 17, radiation requirements depending. Subjects are expected to be involved in this study for approximately 6 weeks from screening discharge.

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
[14C]-RLY-4008 Oral Capsule 70 mg (NMT 4.8 MBq)

Primary outcome(s)
1. Assessment of mass balance measured using urine and faecal samples taken from Day 1 up to Day 17, or until mass balance criteria are met
2. Metabolite profiling and structural identification measured using blood, urine and faecal samples taken from Day -1 up to Day 17, or until mass balance criteria are met

Key secondary outcome(s)
1. Identification of the chemical structure of each metabolite measured using blood, urine and faecal samples taken from Day -1 until Day 17, or until mass balance criteria are met
2. Evaluation of whole blood:plasma concentration ratios for total radioactivity measured using blood samples taken from Day 1 until Day 15
3. Safety and tolerability measured using the incidence of adverse events and serious adverse events, and changes from baseline for vital signs, electrocardiograms and laboratory safety tests from Day -1 until discharge from the study
4. Pharmacokinetic parameters measured using blood samples taken from Day 1 until Day 15

Completion date
19/08/2022

Eligibility

Key inclusion criteria
1. Must provide written informed consent
2. Must be willing and able to communicate and participate in the whole study
3. Aged 30 to 55 years inclusive at the time of signing informed consent
4. Must agree to adhere to the contraception requirements defined in the clinical protocol and have no desire to father children in the next 6 months.
5. Healthy males
6. Body mass index (BMI) of 18.0 to 31.0 kg/m2 as measured at screening
7. Body weight of ≥50 kg as measured at screening
8. Must have regular bowel movements (i.e. average stool production of ≥1 and ≤3 stools per day)

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
30 Years

Upper age limit
55 Years

Sex
Male

Total final enrolment
6

Key exclusion criteria
1. Serious adverse reaction or serious hypersensitivity to any drug or the formulation excipients
2. Has known systemic hypersensitivity to the RLY-4008 drug substance, or inactive ingredients
3. Presence or history of clinically significant allergy requiring treatment, as judged by the investigator. Hay fever is allowed unless it is active
4. History of clinically significant cardiovascular, renal, hepatic, dermatological, chronic respiratory or gastrointestinal disease, neurological or psychiatric disorder, as judged by the investigator
5. History of any retinal disorder (e.g. tears, detachment, retinitis pigmentosa) or symptoms suggestive of such disorder (e.g. history of floaters, distorted vision or blind spots) or history of significant corneal disorder (e.g. corneal ulcer, dry eyes requiring treatment) as assessed by the investigator or delegate at screening

6. Participants who do not have suitable veins for multiple venepunctures/cannulation as assessed by the investigator or delegate at screening
7. Evidence of current SARS-CoV-2 infection within 4 weeks of IMP administration
8. Clinically significant abnormal clinical chemistry, haematology, coagulation or urinalysis as judged by the investigator
9. Positive hepatitis B surface antigen (HBsAg), hepatitis C virus antibody (HCV Ab) or human immunodeficiency virus (HIV) 1 and 2 antibody results
10. Evidence of renal impairment at screening, as indicated by an estimated creatinine clearance (CLcr) of <80 mL/min using the Cockcroft-Gault equation
11. Serum phosphate above the upper limit of the reference range at screening
12. Serum ALT or bilirubin >1.25 upper limit of reference range at screening
13. Participants who have received any IMP in a clinical research study within the 90 days prior to Day 1, or less than 5 elimination half-lives prior to Day 1, whichever is longer
14. 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
15. Donation of blood or plasma within the previous 3 months or loss of greater than 400 mL of blood before IMP administration
16. Participants 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 PD activity is expected by the time of dosing with IMP; and if the use of medication does not jeopardise the safety of the trial participant; and if the use of medication is not considered to interfere with the objectives of the study
17. Participants who have taken any medication known to inhibit or induce CYP3A4 enzymes in the 4 weeks before IMP administration
18. Participants who have had any vaccine, including the COVID-19 vaccine, in the 8 days before IMP administration
19. History of any drug or alcohol abuse in the past 2 years
20. 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)
21. A confirmed positive alcohol breath test at screening or admission
22. 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
23. Current users of e-cigarettes and nicotine replacement products and those who have used these products within the last 12 months
24. Confirmed positive drugs of abuse test result
25. Male participants with pregnant or lactating partners
26. Participants who are, or are immediate family members of, a study site or sponsor employee
27. Failure to satisfy the investigator of fitness to participate for any other reason

Date of first enrolment
12/07/2022

Date of final enrolment
19/08/2022

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Quotient Sciences
Mere Way
Ruddington Fields
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NG11 6JS

Sponsor information

Organisation
Elevar Therapeutics, Inc.

Funder(s)

Funder type
Industry

Funder Name
Relay Therapeutics

Alternative Name(s)
Relay, Relay Therapeutics, Inc., Relay Therapeutics Inc

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
United States of America

Results and Publications

Individual participant data (IPD) sharing plan

The datasets generated and/or analysed during the current study are not expected to be made available because of their high commercial sensitivity and the negligible benefit to the public of publication of results of non-therapeutic clinical trials.

IPD sharing plan summary

Not expected to be made available