ISRCTN11798668 https://doi.org/10.1186/ISRCTN11798668

A two-part study to assess the effectiveness, safety, and blood levels of repeat doses of inhaled ETD001 in people with cystic fibrosis

Submission date
12/07/2023

Recruitment status
No longer recruiting

Registration date
02/04/2024

Overall study status
Completed

Last Edited
13/11/2026

Condition category
Respiratory

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Cystic fibrosis (CF) is an inherited disorder that causes sticky mucus to build up in the lungs and digestive system. Current treatments help control the symptoms, but they don't work for everyone, and some treatments are burdensome. The study drug (called ETD001) works by loosening the mucus in the lungs so it is less sticky making breathing easier and helping to reduce chest infections. ETD001 is given using a device called a nebuliser that turns the liquid medicine into a mist so that it may be breathed in. This study is the first to give ETD001 to people with CF. The study will be run in two parts. Part A will assess if ETD001 is safe to give to people with CF, and Part B will assess if ETD001 improves lung function. The study drug is taken twice a day, in Part A it is taken for 7 days and in Part B for 28 days. In Part B there will be a separate period where dummy medicine is given for 28 days so the treatments can be compared. The study medicine (ETD001 and the dummy medicine) is taken alongside usual prescribed CF medication. Most of the study medicine will be taken at home.

Who can participate?
Adults over 18 years, with CF. Thirty people are needed to complete the study, the study will be run at sites in the United Kingdom, France, Germany and Italy.

What does the study involve?
In Part A participants will receive 13 doses of either ETD001 or placebo, 8 people will take part. Participants will take up to 56 days to finish the study and make 5 outpatient visits.
In Part B participants will receive 55 doses of ETD001 and 55 doses of placebo, 32 people will take part. Participants will take up to 133 days to finish the study and will make 8 outpatient visits.
Study assessments include physical examinations, vital signs, heart traces, blood/urine samples, breathing tests and health questionnaires.

What are the possible benefits and risks of participating?
This is the first study to administer ETD001 to people with CF so there may be no direct medical benefit from taking part, but the information gained from this study may help other people with

CF in the future.
All medications have the potential to cause side effects. ETD001 is an experimental drug, therefore, the risks to human participants have not been fully evaluated. Side effects often go away quickly but it is possible for them to last a long time or be serious. ETD001 has been given to healthy volunteers. Overall, ETD001 was well tolerated and no serious side effects occurred. Of the potential side effects reported, all were mild or moderate in intensity.
Some of the side effects observed, albeit not common included:
• Headache
• Chest discomfort
Other reported side effects included:
• Feeling faint
• Cough
• Shortness of breath
• Muscle or bone pain
• Nasal congestion
• Sore throat
• Pain, burning, or redness of the eyes
Participants will be monitored closely and asked to report any side effects immediately to their study doctor.
Risks from study procedures
Some of the study assessments and tests are similar to those received as part of standard care. They do not have a greater risk than if they were performed outside of the study.
Blood sampling -during the collection of blood samples, participants may experience pain and/or bruising at the needle injection site. Although rare, localised clot formation and infections may occur. Light-headedness and/or fainting may also occur during or shortly after the blood sample is taken.
Electrocardiogram (ECG) - ECG patches may cause a skin reaction such as redness or itching. Participants may also experience skin discomfort and/or hair loss (on the chest) associated with the removal of the patches.
Spirometry: Some participants may feel dizzy, faint, shaky, breathless, sick, or tired for a short period after the tests. The tests may also cause a participant to cough.
All risks associated with the study drug and procedures will be discussed with the study

Where is the study run from?
Enterprise Therapeutics Ltd (UK)

When is the study starting and how long is it expected to run for?
July 2023 to November 2025

Who is funding the study?
Enterprise Therapeutics Ltd (UK)

Who is the main contact?
Paul Russell, info@enterprisetherapeutics.com

Contact information

Type(s)
Scientific

Contact name

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Public

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Additional identifiers

ClinicalTrials.gov (NCT)
NCT06478706

Clinical Trials Information System (CTIS)
2023-504092-25-00

Integrated Research Application System (IRAS)
1008079

Central Portfolio Management System (CPMS)
56452

Protocol serial number
ET-ENAC-03

Study information

Scientific Title

A randomised, double-blind, placebo controlled, two-part study to evaluate the efficacy, safety, tolerability and pharmacokinetics of a repeat dose of inhaled ETD001 in people with cystic fibrosis

Study objectives
Primary Objective:
Part A
1. To assess the safety and tolerability of repeat inhaled doses of ETD001 in pwCF, compared to placebo
Part B
2. To assess the effect of repeat inhaled doses of ETD001 on percent predicted forced expiratory volume in 1 second (ppFEV1) in pwCF, compared to placebo

Secondary Objectives
Part A
1. To characterise the plasma and urine PK following repeat inhaled doses of ETD001 in pwCF
Part B
2. To assess the effect of repeat inhaled doses of ETD001 on other lung function assessments including relative change in ppFEV1, forced vital capacity (FVC), FEV1/FVC ratio and maximal mid- expiratory flow rates (FEF25-75), compared to placebo
3. To assess the effect of repeat inhaled doses of ETD001 on safety and tolerability in pwCF, compared to placebo
4. To assess the effect of repeat inhaled doses of ETD001 on CFQ-R (respiratory domain) in pwCF, compared to placebo
5. To characterise the plasma PK via a population PK (Pop PK) approach following repeat inhaled doses of ETD001 in pwcF

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 14/09/2023, East Midlands - Leicester South Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 207 104 8143; leicestersouth.rec@hra.nhs.uk), ref: 23/EM/0180

Primary study design
Interventional

Study design
Interventional double-blind randomized cross over placebo-controlled trial

Study type(s)
Efficacy, Safety

Health condition(s) or problem(s) studied
Cystic fibrosis

Interventions
Part A (safety and tolerability in participants with cystic fibrosis): Eight participants will receive 13 doses of ETD001 4.5 mg or placebo as an oral inhalation twice a day over 7 days, twice daily

doses on Days 1 to 6 and a single dose on the morning of Day 7. Six participants will receive active ETD001 and 2 will receive placebo. Allocation of participants to treatment type will be coordinated using a centralised interactive response technology (IRT) system.
Part B (safety and efficacy in participants with cystic fibrosis): Thirty-two participants will be required to complete two 28-day treatment periods, twice daily doses of ETD001 4.5 mg will be administered in one treatment period and twice daily doses of placebo will be administered in the other treatment period. In each treatment period, a total of 55 doses of ETD001 4.5 mg or placebo will be administered as an oral inhalation over 28 days, twice daily doses on Days 1 to 27 and a single morning dose on the morning of Day 28. The order in which participants receive ETD001 and placebo will be coordinated using the centralised IRT system.
All study participants, in both Part A and Part B, will return to the study centre for a safety follow-up appointment 3 weeks (21 days) after completing the final treatment period.
A review of safety data from Part A will be completed by an independent data safety monitoring board before the start of Part B. Participants who have completed Part A may also take part in Part B.

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
ETD001

Primary outcome(s)
Part A
1. Number of participants reporting adverse events (AE) – baseline to follow up (approximately 28 days)
2. Number of participants who discontinue due to an AE – baseline to follow up (approximately 28 days)
3. Number of participants with vital sign abnormalities as assessed by measuring systolic and diastolic blood pressure, heart rate, respiration rate, temperature and peripheral oxygen saturation – baseline to follow up (approximately 28 days)
4. Number of participants with spirometry abnormalities as measured using a spirometer – baseline to follow up (approximately 28 days)
5. Number of participants with laboratory test abnormalities measured using biological samples – baseline to follow up (approximately 28 days)
6. Number of participants with electrocardiogram (ECG) abnormalities measured using 12-Lead ECG recordings – baseline to follow up (approximately 28 days)

Part B
7. Absolute change in percent predicted forced expiratory flow volume over 1 second (ppFEV1) measured using a spirometer from Day 1 to Day 28 in Treatment Period 1 and Treatment Period 2 (approximately 84 days)

Key secondary outcome(s)
Part A
1. Plasma concentrations and derived PK parameters (Cmax, Tmax , AUC(0-t), AUC(0-tau), AUC(0-inf), Tlast, λz, T1/2, CL/F, Vz/F) of ETD001 measured in blood samples collected at specific timepoints pre-dose and post-dose on Day 1 and up to 21 days after the final dose of study

medication (approximately 28 days)
2. Urine concentrations (amount excreted in urine (Ae); fraction of dose excreted (Fe), renal clearance (CL)), of ETD001 measured in urine samples collected at specific timepoints pre-dose and up to 6 hours post-dose on Day 1 (1 day)

Part B
3. Relative change in ppFEV1 measured using a spirometer from Day 1 to Day 28 in Treatment Period 1 and Treatment Period 2 (approximately 84 days)
4. Absolute change in other lung function parameters (FVC, FEV1/FVC ratio and FEF25-75) measured using a spirometer from Day 1 to Day 28 in Treatment Period 1 and Treatment Period 2 (approximately 84 days)
5. Number of participants reporting adverse events (AE) – baseline to follow up (approximately 105 days)
6. Number of participants who discontinue due to an AE – baseline to follow up (approximately 105 days)
7. Number of participants with vital sign abnormalities as assessed by measuring systolic and diastolic blood pressure, heart rate, respiration rate, temperature and peripheral oxygen saturation from Day 1 to Day 28 in Treatment Period 1 and Treatment Period 2 and up to 21 days after the final dose of study medication (approximately 105 days)
8. Number of participants with laboratory test abnormalities measured using biological samples from Day 1 to Day 28 in Treatment Period 1 and Treatment Period 2 and up to 21 days after the final dose of study medication (approximately 105 days)
9. Number of participants with electrocardiogram (ECG) abnormalities measured using 12-Lead ECG recordings from Day 1 to Day 28 in Treatment Period 1 and Treatment Period 2 and up to 21 days after the final dose of study medication (approximately 105 days)
10. Change in Cystic Fibrosis Questionnaire – Revised (CFQ-R) from Day 1 to Day 28 in Treatment Period 1 and Treatment Period 2 (approximately 84 days)
11. Population PK characteristics and model generated individual PK parameters (Cmax, Tmax , AUC(0-t), AUC(0-tau), AUC(0-inf), Tlast, λz, T1/2, CL/F, Vz/F) of ETD001 measured in blood samples collected at specific timepoints pre-dose and post-dose on Day 1 and up to 21 days after the final dose of study medication (approximately 105 days)

Completion date
14/11/2025

Eligibility

Key inclusion criteria
1. All genders ≥18 years of age, who fit one of the following criteria: Women of childbearing potential who are willing and able to use contraception from a minimum of 28 days before receipt of the first dose of study medication until completion of the final follow-up visit. Women of non-childbearing potential defined as being amenorrhoeic for >12 months with an appropriate clinical profile (e.g. age appropriate, menopausal symptoms). However, if indicated, this should be confirmed by follicle-stimulating hormone levels consistent with menopause (according to local laboratory ranges). Alternatively, women without a uterus or who have been permanently sterilised (e.g. hysterectomy, bilateral salpingectomy or bilateral oophorectomy, but not tubal ligation). Men who are willing and able to use one of the contraception methods from the time of the first dose, until completion of the final follow up visit
2. Have a confirmed diagnosis of CF [positive sweat chloride value ≥ 60 mEq/L (by quantitative pilocarpine iontophoresis) and/or genotype with two identifiable mutations consistent with CF, accompanied by one or more clinical features consistent with the CF phenotype].

3. Have a FEV1 ≥ 40% and ≤ 90% of predicted normal for age, gender, and height using Global Lung Function Initiative (GLI) standards.
4. Be able to reproducibly perform spirometry manoeuvres (i.e., able to perform at least three acceptable forced expiratory curves based on the investigator's assessment).
5.Clinically stable CF lung disease, defined as no documented decrease in FEV1 > 10%, or signs and symptoms of acute pulmonary exacerbation such as: increased cough, change in sputum (volume or consistency), change in respiratory examination and respiratory rate, decreased appetite or weight loss, chest pain, hemoptysis, decreased lung function, fever defined as temperature > 38°C (100.4°F) within 28 days prior to Visit 1.
6. Routine CF therapy (bronchodilator, anti-inflammatory, inhaled corticosteroid, physiotherapy technique/schedule (including use of vibrating vests etc.) has not changed (in dose or medication) within 28 days prior to Visit 1.
7. Provided written informed consent.
8. Be able and willing to follow instructions and complete study procedures and be willing to comply with the study protocol and study drug use.
9. Females must have a negative serum β human chorionic gonadotropin (β-hCG) at Visit 1
10. Be able to use a nebuliser.
11. Body mass index (BMI) > 16 and < 30 kg/m²

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 Years

Upper age limit
100 Years

Sex
All

Total final enrolment
57

Key exclusion criteria
1. Abnormal liver function defined as any 2 or more of the following: ≥3 × upper limit of normal (ULN) aspartate aminotransferase (AST), ≥3 × ULN alanine aminotransferase (ALT), ≥3 × ULN gamma-glutamyl transpeptidase (GGT), ≥3 × ULN alkaline phosphatase (ALP), or ≥2 × ULN total bilirubin
2. Abnormal renal function defined as glomerular filtration rate ≤50 mL/min/1.73 m²
3. People with a history of any solid organ transplantation
4. Have a historical chest x-ray (anterior/posterior view) within the past 12 months with abnormalities suggesting unstable pulmonary disease other than CF
5. Received CFTR modulator therapy in the 60 days before Visit 1
6. Have changes in bronchodilator, corticosteroid or other anti-inflammatory medications 14

days prior to and inclusive of Visit 1
7. Be unable to withhold use of long-acting bronchodilators 24 hours prior to spirometry or unable to withhold short-acting bronchodilator within 6 hours prior to spirometry
8. Be unable to withhold use of anti-cholinergics within 24 hours of spirometry
9. Have started using dornase alfa, hypertonic saline, or other airway clearing therapy less than 28 days prior to Visit 1
10. Using inhaled antibiotics for less than 2 complete cycles and unable to complete the entire study during the off or on cycle
11. Have changes in inhaled or oral antibiotic use within 14 days prior to and inclusive of Visit 1
12. Be taking oral corticosteroids (prednisone equivalents) within 14 days prior to and inclusive of Visit 1, exceeding 10 mg per day or 20 mg every other day
13. Used diuretics, or renin-angiotensin aldosterone system antihypertensive drugs (spironolactone, angiotensin-converting enzyme (ACE) inhibitors, or angiotensin receptor blockers (ARB)), drospirenone, or trimethoprim in the 28 days prior to Visit 1, or an anticipated need for any of these medications during the study
14. Presence of co-morbidities and medical history listed below, or in the opinion of the investigator, may pose additional risk by participating in the study, or may confound the results of the study:
14.1. Cirrhosis with portal hypertension (e.g., splenomegaly, oesophageal varices)
14.2. Past or present positive sputum culture for organisms that are often associated with a faster decline in pulmonary status is allowed if, in the opinion of the investigator, clinical stability has not been adversely affected. Subjects with these organisms can remain on chronic treatment for them if applicable, as long as the medications are not prohibited in this study. To assure clinical stability, treatment for these organisms should start at least 8 weeks before screening, and the subjects will be expected to continue the treatment through the final study visit.
14.3. History of malignancy within past 5 years (except for excised basal cell carcinoma of the skin with no recurrence, or treated carcinoma in situ of the cervix with no recurrence).
14.4. Abuse or suspected abuse of alcohol, medications, or illicit drugs within 1 year before Screening, per the investigator.
14.5. Psychiatric condition that makes it unlikely that the course of treatment or follow-up will be completed.
14.6. Smoking or vaping tobacco or cannabis products within 1 year before Screening.
14.7. Need for supplemental oxygen while awake, or > 2 L/minute while sleeping.
14.8. Recent significant weight loss, defined as 2 kg loss within the 4 weeks prior to screening.
14.9. Severe CF related diabetes mellitus with poor glucose control, microvascular complications or microalbuminuria.
14.10. History or current evidence of any clinically significant cardiac (eg, heart failure, left ventricular hypertrophy, myocardial infarction, and unstable arrhythmia) or prolonged QTcF >450 msec at screening.
15. Serum potassium > ULN in non-haemolysed sample, at Visit
16. History of significant intolerance to inhaled hypertonic saline (HS) or dornase alfa
17. Is pregnant, breast-feeding or intending to become pregnant before or during the study, or before completing the final follow up visit
18. Received an experimental drug or used an experimental medical device within 30 days or within a period less than five times the drug's half-life, whichever is longer, before the first dose of the study drug is scheduled
19. Allergy to any of the active or inactive ingredients in the study medication
20. Participant is mentally or legally incapacitated or legally institutionalised
21. Participant is an employee of the Sponsor or contract research organisation (CRO), or a relative of an employee of the Sponsor or CRO
22. A positive test for HIV-1 & -2 antibodies or positive hepatitis C antibody result or a positive

hepatitis B surface antigen at Visit 1 or anytime

Date of first enrolment
26/06/2024

Date of final enrolment
15/08/2025

Locations

Countries of recruitment
United Kingdom

England

Northern Ireland

Scotland

Wales

France

Germany

Italy

Study participating centre
Royal Brompton Hospital
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SW3 6NP

Study participating centre
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Study participating centre
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Study participating centre
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Study participating centre
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Study participating centre
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Sponsor information

Organisation
Enterprise Therapeutics Ltd

Funder(s)

Funder type
Industry

Funder Name
Enterprise Therapeutics Ltd

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Other unpublished results	version 1	14/08/2026	13/11/2026	No	No
Plain English results	version 1	28/07/2026	13/11/2026	No	Yes