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A study to learn how the study medicine called PF-07868489 is tolerated and acts in people with pulmonary arterial hypertension

Submission date 27/11/2024	**Recruitment status** Recruiting	[X] Prospectively registered [X] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 27/03/2025	**Overall study status** Ongoing	
Last Edited 20/06/2025	**Condition category** Circulatory System	

Plain English summary of protocol

Background and study aims
A study to learn how the study medicine called PF-07868489 is tolerated and acts in people with pulmonary arterial hypertension.

Who can participate?
To join this study, participants must be 18 or older and agree to all study requirements. They need a confirmed diagnosis of pulmonary arterial hypertension (PAH) and must fit specific PAH subtypes. Their PAH should be classified as WHO functional class II or III. Participants must have certain heart and lung function measurements and a stable treatment plan for PAH. They should also have a body mass index (BMI) between 16 and 35. Additionally, they need to be able to walk a specific distance in six minutes and have no other significant lung diseases.

What does the study involve?
Not provided at time of registration

What are the possible benefits and risks of participating?
Benefits:
Not provided at time of registration

Risks:
Taking part in this study has some risks. The study drug(s) or procedure(s) may make participants feel unwell or uncomfortable or could be harmful.
Participants who receive PF-07868489 are at risk for anaphylaxis and injection site reactions. PF-07868489 induces significant antibody responses, by blocking harmful BMP9 activity in the lungs. Adverse reactions expected after receiving the Investigational medicinal product is projected to be low. Participants will be observed closely for signs and symptoms of immunogenicity using standard clinical monitoring. Injection site reactions will be documented as adverse events. For SC administration of study treatment, injection site reactions will be monitored, and injection sites rotated.
Participants may experience bleeding, arrythmias, lung collapse and death related to the RHC

procedure, which is an invasive procedure that involves insertion of a catheter into a major vein, through the right atrium and ventricle, and into the pulmonary vasculature. RHC will only be performed by personnel skilled in performing RHC, to manage potential complications.
There may be other risks that are currently unknown because the study drug is still being investigated.
Participants will be instructed to immediately inform the study doctor or staff if they experience any of these symptoms: trouble breathing, or swelling of the face, mouth, lips, gums, tongue, or neck. For other allergic reactions which may include rash, hives, blisters or any others which can be severe, the study doctor will determine if a patient needs extra procedures or medicines to help manage the side effects.
PF-07868489 would not be given to pregnant women or women who are breastfeeding. Currently, the effects of PF-07868489 on male and female fertility, pregnancy in humans, and effects on a foetus or a nursing child are not known. Sexually active female participants must use contraception consistently and correctly during the study and for at least 15 weeks after the last dose of the study drug. Females who are pregnant, planning on becoming pregnant, or breastfeeding an infant will not be included in the study.
Participants will undergo a right heart catheterisation (RHC) at screening and week 24 (end of treatment) visit which would require exposure to X-ray. The total protocol dose (TPD) would be approximately 8.7 mSv. This is equivalent to around 4 years of natural background radiation exposure in the UK. Ionising radiation can cause cancer which manifests itself after many years or decades. The risk of developing cancer because of taking part in this study is estimated as 0.05%, extremely small. For comparison, the natural lifetime cancer incidence in the general population is about 50%.

Where is the study run from?
Pfizer (USA)

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

Who is funding the study?
Pfizer (USA)

Who is the main contact?
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Contact information

Type(s)
Public, Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
2024-514064-17

Integrated Research Application System (IRAS)
1010510

ClinicalTrials.gov (NCT)
NCT06137742

Protocol serial number
C5001001, CPMS 59297

Study information

Scientific Title
A phase I/II, randomized, double-blind, placebo-controlled study to evaluate the safety, tolerability, pharmacokinetics, and pharmacodynamics of single escalating doses of PF-07868489 in healthy adult participants and, additionally, clinical activity of repeat doses in participants with pulmonary arterial hypertension

Study objectives
Primary objectives:
1. To evaluate the safety and tolerability of repeat SC doses of PF-07868489 in participants with PAH.
2. To characterize change in blood concentration of NTproBNP following repeat SC dose administration of PF- 07868489 in participants with PAH.

Secondary objectives:
1. To characterize serum exposure following repeat SC doses of PF-07868489 in participants with PAH.
2. To evaluate the immunogenicity profile of PF-07868489 following repeat SC doses in

participants with PAH.
3. To evaluate the effects of repeated PF-07868489 dosing on 6MWD and PVR in participants with PAH.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 03/02/2025, East of England - Cambridgeshire and Hertfordshire Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 (0)20 7104 8096; cambsandherts.rec@hra.nhs.uk), ref: 24/EE/0275

Study design
Interventional double-blind randomized parallel-group placebo-controlled trial

Primary study design
Interventional

Study type(s)
Safety, Efficacy

Health condition(s) or problem(s) studied
Pulmonary arterial hypertension

Interventions
This is a Phase I/II, randomized, double-blind, placebo-controlled study conducted in 2 sequential parts. Part A is designed to evaluate the safety, tolerability, PK, and immunogenicity of single escalating doses of PF-07868489 in healthy adult participants. (Not Applicable to the UK, just for information.)

Part B is a 24-week part designed to evaluate the clinical activity, safety, tolerability, PK, immunogenicity, and PD of repeat doses of PF-07868489 in participants with PAH. It is not known if participants with PAH will derive clinical benefit from exposure to PF-07868489 but they may. Up to approximately 36 participants will be randomized into Part B of this study.

The study design, inclusion/exclusion criteria, and procedures have been developed in a manner to minimize the risks to participants. Evidence for potential benefits comes from data observed in rodent models of PAH and human genetic evidence suggesting a role for altered BMP9 receptor signalling in the pathogenesis of PAH.
The patient phase (Part B) of the study will only be initiated after adequate safety and tolerability have been established in healthy participants and the GLP chronic toxicity data are available. Evaluation of emerging, preliminary clinical data from Part A of the study has not identified any safety or tolerability issue that would preclude progression into Part B of the study in patients with PAH. Additionally, emerging unblinded safety data from Part B of the study will be monitored periodically by an internal review committee that will provide feedback on the emerging safety profile in participants with PAH.

Following the Screening period of up to 35 days to confirm eligibility, participants with PAH who meet all eligibility criteria at Screening and Baseline will be randomized to study intervention (PF-07868489 or placebo) in a 1:1 ratio.

Beginning on Day 1, participants will receive a total of 6 doses administered Q4W SC (through Week 20). Following Day 1, there will be a visit at Week 1 (Day 8) for initial safety monitoring followed by visits at Week 4 and Q4W thereafter. The active treatment period is defined as extending from Day 1 through the Week 24 / EOT visit.
PF-07868489 drug product is provided as a 100 mg/mL solution/suspension for injection.

Participants who complete the active treatment period of study C5001001 may be offered the opportunity to enrol in an OLE study. All participants in the OLE study will receive active study intervention (details of the OLE study will be provided in a separate protocol).

During the site visits, the following procedures may occur:
Vital Signs
Physical Exam
ECG
Blood samples
Contraception discussion
Pregnancy test (if applicable)
X-RAY
Chest CT-Scan
Study drug administration
Questionnaires etc.

An independent oversight committee in the form of an IRC will monitor unblinded safety and tolerability data of PF-07868489 in the participants in Part B of the study on an ongoing, regularly scheduled basis. The IRC may also be charged with the performance of any planned or unplanned IAs. Additional details will be described in the IRC charter.

Intervention Type
Drug

Phase
Phase I/II

Drug/device/biological/vaccine name(s)
PF-07868489

Primary outcome(s)
1. Incidence and severity of AE and SAEs
2. Change from baseline in vital signs
3. Change from baseline in clinical laboratory values.- Change from baseline in ECG parameters (heart rate, QT, QTcF, PR, and QRS intervals)
4. Change from baseline at Week 24 of NTproBNP

Key secondary outcome(s))
1. PF-07868489 PK parameters after repeat doses; as data permit: Cmin, and t1/2
2. Incidence of the development of ADA against PF-07868489 following repeat doses
3. Change from baseline at Week 24 on 6MWD
4. Change from baseline at Week 24 on PVR

Completion date
12/01/2027

Eligibility

Key inclusion criteria

1. Participants aged ≥18 years (or the minimum age of consent in accordance with local regulations) at screening who have signed informed consent.
2. Participants who are willing and able to comply with all scheduled visits, treatment plan, laboratory tests, lifestyle considerations, and other study procedures.
3. Documented diagnostic RHC prior to Screening confirming diagnosis of PAH (WHO Group 1 PH) including any of the following subtypes:
- Idiopathic or heritable PAH.
- Drug- or toxin-induced PAH.
- PAH associated with connective tissue disease.
- PAH associated with simple, congenital systemic-to-pulmonary shunts at least 1 year following shunt repair.
4. PAH classified as WHO functional class II or III.
5. Pre-randomization RHC documenting a minimum of PVR ≥ 400 dyn sec/cm\(^5\) (5 Wood units); and no contraindication to RHC. RHC performed within 12 weeks of Screening as part of the participants management of PAH can satisfy this criterion, if the requisite hemodynamic data are available. Otherwise, a RHC needs to be performed prior to randomization. In this case, the RHC should only be performed if the potential participant meets all other inclusion /exclusion criteria for eligibility.
6. PFTs (spirometry) performed as part of the diagnostic evaluation of PAH excluding clinically relevant obstructive or restrictive pulmonary physiology (unless the participant is an active smoker of > 10 cigarettes/equivalent per day or a smoking history ≥10 pack-years, in which case, the PFTs should be done within 6 months prior to Screening). A high-resolution chest computed tomography within 1 year of Screening indicating no more than minimum emphysematous or interstitial changes may be used to satisfy this requirement.
7. Documentation in the participant's medical history that CTEPH has been excluded.
8. 6MWD ≥ 150 m and ≤ 500 m repeated at least twice during Screening and top two values within 15% of each other, calculated from the highest value.
9. A stable dose of at least 2 SOC PAH vasodilator class therapies for 60 days prior to Screening.
- Titration of IV/SC prostanoids are permitted within 10% of optimal dose in accordance with standard of care.
10. BMI 16 to 35 kg/m²

Participant type(s)

Patient

Healthy volunteers allowed

No

Age group

Adult

Lower age limit

18 years

Sex

All

Key exclusion criteria
1. Any medical or psychiatric condition including recent (within the past year) or active suicidal ideation/behaviour or laboratory abnormality that may increase the risk of study participation or, in the investigator's judgment, make the participant inappropriate for the study.
2. Systolic BP < 90 mmHg during Screening or at baseline.
3. ECG with QTcF > 490 msec during Screening or Randomization.
4. Any of the following clinical chemistry values during Screening:
- Alanine aminotransferase (ALT) or aspartate aminotransferase (AST) > 3 × ULN (> 5 ULN if solely due to right heart failure) or total bilirubin ≥ 2 × ULN (For Gilbert's syndrome, direct bilirubin > ULN [or ≥ 2 × ULN if solely due to right heart failure] is exclusionary)
- eGFR < 30 mL/min/1.73 m^2 within 30 days prior to randomization or required renal replacement therapy within 90 days of randomization.
5. Hematologic abnormalities defined as:
- Platelets ≤ 50,000/mm^3
6. Participants with a diagnosis of COPD or other clinically significant lung disease.
7. Stopped receiving pulmonary hypertension chronic general supportive therapy (e.g., diuretics, oxygen, anticoagulants, digoxin) within 90 days prior to Screening.
8. History of atrial septostomy within 180 days prior to Screening.
9. Pulmonary capillary wedge pressure (PCWP)/Pulmonary Arterial Occlusion Pressure (PAOP) > 15 mmHg on RHC conducted during Screening.
10. History of severe allergic or anaphylactic reaction or hypersensitivity to recombinant proteins or excipients in investigational product.
11. History of clinically significant (as determined by the investigator) non-PAH related cardiac, endocrine, hematologic, hepatic, immune, metabolic, urologic, pulmonary, neurologic, neuromuscular, dermatologic, psychiatric, renal, and/or other disease that may limit participation in the study.
12. Current use of any prohibited concomitant medication(s) or participants unwilling or unable to use a required concomitant medication(s).
13. Previous administration with an investigational drug within 30 days (or as determined by the local requirement) or 5 half-lives preceding the first dose of study intervention used in this study (whichever is longer) and not concurrently involved in a clinical trial with another investigational product during the study.
14. Uncontrolled systemic hypertension as evidenced by sitting systolic BP > 160 mmHg or sitting diastolic BP > 100 mmHg during Screening after a period of rest.

Date of first enrolment
07/06/2025

Date of final enrolment
12/01/2027

Locations

Countries of recruitment
United Kingdom

England

Scotland

Australia

Belgium

Canada

China

Czech Republic

France

Germany

Greece

Italy

Japan

Korea, South

Spain

Study participating centre
Hammersmith Hospital
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Study participating centre
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Study participating centre
Golden Jubilee National Hospital
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Sponsor information

Organisation
Pfizer Europe MA EEIG

Funder(s)

Funder type
Industry

Funder Name
Pfizer

Alternative Name(s)
Pfizer Inc., Pfizer Consumer Healthcare, Davis, Charles Pfizer & Company, Warner-Lambert, King Pharmaceuticals, Wyeth Pharmaceuticals, Seagen, Pfizer 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 during and/or after, are analysed during the current study will be stored in a non-publicly available repository (The identity of all participating patients (sufficient information to link records e.g., CRFs and hospital records), all original signed informed consent /assent documents, copies of all CRFs, safety reporting forms, source documents, and detailed records of treatment disposition, and adequate documentation of relevant correspondence (e. g., letters, meeting minutes, and telephone call reports). The records should be retained by the

investigator according to ICH guidelines, according to local regulations, or as specified in the clinical study agreement (CSA), whichever is longer. The investigator must ensure that the records continue to be stored securely for so long as they are retained. If the investigator becomes unable for any reason to continue to retain study records for the required period (e.g., retirement, relocation), Pfizer should be prospectively notified. The study records must be transferred to a designee acceptable to Pfizer, such as another investigator, another institution, or to an independent third party arranged by Pfizer. Investigator records must be kept for a minimum of 15 years after completion or discontinuation of the study or for longer if required by applicable local regulations. The investigator must obtain Pfizer's written permission before disposing of any records, even if retention requirements have been met.

IPD sharing plan summary

Stored in non-publicly available repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet		16/10/2024	13/12/2024	No	Yes
Participant information sheet		16/10/2024	13/12/2024	No	Yes
Protocol file		23/09/2024	13/12/2024	No	No