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A clinical study to investigate the safety and tolerability of efimosfermin alfa injection in participants with known or suspected F2- or F3-stage metabolic dysfunction-associated steatohepatitis (BOS-580-302)

Submission date 10/03/2026	**Recruitment status** Recruiting	[ ] Prospectively registered [ ] Protocol [ ] Statistical analysis plan [ ] Results [ ] Individual participant data [X] Record updated in last year
Registration date 03/07/2026	**Overall study status** Ongoing	
Last Edited 03/07/2026	**Condition category** Digestive System	

Plain English summary of protocol

Background and study aims
Metabolic dysfunction-associated steatohepatitis (MASH) is liver inflammation and damage caused by a buildup of fat in the liver. This is a study of the safety and tolerability of efimosfermin administered every 4weeks by injection in adult patients with MASH.

Who can participate?
Patients aged 18 to 75 years with known or suspected MASH with fibrosis consistent with stage F2 or F3

What does the study involve?
Participants are randomized to receive 225mg efimosfermin, 300mg efimosfermin, or placebo every 4weeks by injection for a period of 52weeks, followed by a final safety follow-up assessment at Week 56. Total time of participation in the study, inclusive of a screening period of up to 8 weeks, is approximately 60 weeks.

What are the possible benefits and risks of participating?
During this study, you will have regular health check-ups. There may or may not be direct benefit for you in taking part in this study. However, during the study, your health will be monitored closely at study visits, and knowledge from this study may also help doctors and researchers learn more about MASH and its treatment. This study helps to learn more about MASH and the effects of the study drug. Your participation will help to understand MASH better and make new treatments for other people living with the same condition.
The most common (occurring in more than 1 in 10 people) side effects for those who took the study drug include nausea, vomiting, diarrhoea, injection site pain, redness, and rashes. In previous studies with efimosfermin, nausea and vomiting were mild in severity and, most of the time, resolved without any treatment. Some participants in other studies with efimosfermin

showed blood test results with high levels of liver proteins that required additional monitoring. There is a possible risk of gallbladder inflammation or symptoms of gallstones. Changes in bone health (decreased bone density due to loss of minerals) have been seen in clinical studies with other drugs that work like efimosfermin. In human studies up to 24 weeks, no meaningful changes in bone tests have been seen. Efimosfermin works in a way that is similar to a natural signal in the body that affects levels of some hormones, such as cortisol. Side effects suggesting changes in cortisol have not been seen in people taking efimosfermin to date. As with other medications, efimosfermin may cause an immune or allergic reaction. Severe allergic reactions are very rare, but life-threatening or fatal reactions can happen.

Where is the study run from?
GlaxoSmithKline (UK)

When is the study starting and how long is it expected to run for?
October 2025 to October 2031

Who is funding the study?
Boston Pharmaceuticals (USA)

Who is the main contact?
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Contact information

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Scientific, Public

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Additional identifiers

ClinicalTrials.gov (NCT)
NCT07221188

Integrated Research Application System (IRAS)
1013370

Sponsor's protocol code number
306246

Study information

Scientific Title
A Phase III, randomized, double-blind, placebo-controlled, three-arm study to investigate the safety and tolerability of efimosfermin alfa in participants with known or suspected F2- or F3-Stage metabolic dysfunction-associated steatohepatitis (MASH) (ZENITH-2)

Acronym
ZENITH-2

Study objectives
Primary objective:
To assess the effects of efimosfermin on safety and tolerability.

Secondary objectives:
1. To assess the effects of efimosfermin on ELF score.
2. To assess the effects of efimosfermin on VCTE-LSM score.
3. To assess the effects of efimosfermin on MRE score.
4. To assess the effects of efimosfermin on HFF and ALT normalization.
5. To assess the effects of efimosfermin on glycemic and metabolic biomarkers.
6. To assess the effects of efimosfermin on lipids.
7. To assess the immunogenicity of efimosfermin.

Ethics approval required
Ethics approval required

Ethics approval(s)
Submitted 19/03/2026, London – London Bridge REC (-, -, -, United Kingdom; -; londonbridge.rec@hra.nhs.uk), ref: -

Primary study design
Interventional

Allocation
Randomized controlled trial

Masking
Blinded (masking used)

Control
Placebo

Assignment
Single

Purpose
Treatment

Study type(s)

Health condition(s) or problem(s) studied
Metabolic dysfunction-associated steatohepatitis (MASH)

Interventions
Participants will be randomized in a 2:2:1 ratio to receive 225 mg efimosfermin, 300 mg efimosfermin, or placebo. The study drug will be administered and dispensed at study visits Q4W for a period of up to 52 weeks. The total time of participation in the study, inclusive of screening and safety follow-up, is approximately 64 weeks.

Since injection volumes for the 225-mg and 300-mg efimosfermin arms are 1.5 ml and 2.0 ml, respectively, additional measures will be implemented to preserve the study blind. Instructions are provided in the pharmacy manual. Criteria are established in this protocol for dose interruption, modification, discontinuation, and resumption based on investigator discretion and following consultation with the study medical monitor (the sponsor or designee) in specific circumstances.

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
Efimosfermin alfa

Primary outcome(s)
Safety and tolerability of efimosfermin measured using the incidence and severity of treatment-emergent adverse events (TEAEs) at week 52

Key secondary outcome(s)
1. Liver fibrosis measured using enhanced liver fibrosis (ELF) score at baseline and week 52
2. Liver stiffness measured using vibration-controlled transient elastography (VCTE) at baseline and week 52
3. Liver stiffness measured using magnetic resonance elastography (MRE) at week 52
4. Hepatic fat fraction (HFF) and alanine aminotransferase (ALT) normalization assessed by measuring HFF by MRI-derived proton density fat fraction (MRI-PDFF) and changes in ALT, AST (aspartate aminotransferase), and ALT/AST ratio at week 52
5. Glycemic and metabolic biomarkers assessed by measuring change in glycated hemoglobin (HbA1c) for participants with type 2 diabetes mellitus (T2DM) at week 52

6. Lipids measured using measuring changes in fasting cholesterol, low-density lipoprotein (LDL-C), high-density lipoprotein C (HDL-C), and fasting triglycerides at Week 52
7. Immunogenicity of efimosfermin assessed by measuring the incidence of ADAs (anti-drug and anti-FGF21 antibodies) at week 52
8. Steady-state pharmacokinetics (PK) of efimosfermin assessed by measuring efimosfermin serum concentrations in participants with PK data following multiple doses at week 52
9. Markers for liver fibrosis, inflammation, and injury assessed by measuring Pro-C3 (type III collagen propeptide), CTX-3 (type III collagen C-telopeptide), Pro-C3/CTX-3 ratio, hsCRP (high sensitivity C-reactive protein), AGILE3+ (3-class diagnosis of liver disease severity), FIB-4 (fibrosis 4), and MAST (magnetic resonance imaging-alanine aminotransferase) at week 52
10. Cardiovascular biomarkers assessed by measuring changes in non-HDL cholesterol, remnant cholesterol, and ApoB10 (apolipoprotein B 100) at week 52
11. Glycemic and metabolic biomarkers assessed by measuring changes in fasting plasma glucose (FPG), insulin and C-peptide levels, waist circumference, adiponectin levels, and homeostatic model assessment of insulin resistance (HOMA-IR) score at week 52.
12. The effect of genetic variation on the effects of efimosfermin may be measured by conducting genetic analysis to evaluate the relationship of genetic variation to safety and efficacy endpoints in the subset of participants who agree to DNA analysis at week 52.
13. The effects of covariates such as demographics on the PK of efimosfermin will be measured by population PK model-derived steady-state PK parameters of the population and participants with PK data including, but not limited to, Cmax (maximum serum drug concentration), AUC (area under the serum concentration-time curve), Cavg (average plasma concentration), and Ctrough (serum concentration of study drug at the end of the dosing interval) at week 52.
14. The relationship between PK and biomarker, safety, and/or efficacy responses will be measured by population PK-PD (pharmacodynamic) modelling conducted using nonlinear mixed effects methods to elucidate an exposure-response relationship with biomarkers, efficacy (clinical outcomes), and safety endpoints as data permit at week 52.

Completion date
31/10/2031

Eligibility

Key inclusion criteria
1. Able and willing to understand and sign a written informed consent form (ICF) that must be obtained prior to the initiation of study procedures
2. Age >=18 through <=75 years at enrolment
3. History or presence of 2 or more of the 5 components of metabolic syndrome per American Heart Association definition
4. History or presence of known or suspected MASH

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 Years

Upper age limit

75 Years

Sex
All

Total final enrolment
0

Key exclusion criteria
1. ALT or AST >=5 × upper limit of normal (ULN).
2. Total bilirubin (BILI) >=1.3 mg/dl. Individuals with documented Gilbert's syndrome may be enrolled if they experienced an isolated increase in total BILI of >=1.3 mg/dL and direct BILI is <=20% of total BILI; otherwise, the individual will be excluded.
3. Serum albumin <=3.5 g/dl
4. International normalized ratio (INR) >=1.3 not due to therapeutic anticoagulation. Individuals receiving chronic anticoagulant treatment with higher INR values may be enrolled at the discretion of the Investigator and Study Medical Monitor.
5. Alkaline phosphatase (ALP) >=2 × ULN
6. Platelet (PLT) count <140,000/mm³; individuals with a PLT count between 110,000/mm³ and 140,000/mm³ may be enrolled after discussion with the Study Medical Monitor
7. Serum creatinine >=1.5 mg/dL or creatinine clearance <=60 ml/min/1.73 m² by the Chronic Kidney Disease Epidemiology Collaboration equation.
8. HbA1c >=9.0%
9. International normalized ratio (INR) >=1.3 not due to therapeutic anticoagulation. Individuals receiving chronic anticoagulant treatment with Model for End-Stage Liver Disease (MELD) 3.0 score >=12 unless the score is elevated in the absence of liver dysfunction (eg, Gilbert's syndrome).
10. Phosphatidylethanol (PEth) >=80 ng/ml at screening.
11. Known co-infection with any of the following:
11.1. Human immunodeficiency virus
11.2. Hepatitis B virus
11.3. Hepatitis C virus (HCV)
11.4. Hepatitis D virus
11.5. Hepatitis E virus
12. Chronic liver disease from any other cause including, but not limited to, alcoholic liver disease; evidence of portal hypertension; viral hepatitis, or any history or evidence of cirrhosis; or decompensated liver disease such as clinical ascites, bleeding gastroesophageal varices, hepatorenal syndrome, or hepatic encephalopathy prior to Screening or Day 1.
13. Current or history of excessive alcohol intake for >=3 months within the 12-month period prior to Screening

Date of first enrolment
24/10/2025

Date of final enrolment
23/04/2027

Locations

Countries of recruitment
United Kingdom

England

Argentina

Australia

Austria

Belgium

Brazil

Bulgaria

Canada

Chile

China

France

Germany

Greece

Hong Kong

India

Israel

Italy

Japan

Korea, South

Mexico

Netherlands

New Zealand

Poland

Saudi Arabia

Singapore

Spain

Taiwan

United States of America

Study participating centre
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Sponsor information

Organisation
GlaxoSmithKline (United Kingdom)

ROR
https://ror.org/01xsqw823

Funder(s)

Funder type

Funder Name
Boston Pharmaceuticals

Alternative Name(s)
Boston Pharmaceuticals Inc.

Funding Body Type
Private sector organisation

Funding Body Subtype
For-profit companies (industry)

Location
United States of America

Results and Publications

Individual participant data (IPD) sharing plan
Information related to this research project will be shared with the following types of organisations:
1. GSK staff, people working on behalf of GSK, and others may check the study records. This is done to make sure that the study is carried out in compliance with legal and quality requirements. For this purpose, people acting on behalf of GSK may view the data in person at the study location or by a video/audio call or securely share documents to a computer system without transferring the file or making a copy of it. Appropriate measures will be taken to protect patients' personal information. No personal information used for study monitoring will be retained by GSK staff or others acting on behalf of GSK.
2. Regulatory agencies, such as the US Food and Drug Administration (FDA), European Medicines Agency (EMA), Medicines and Healthcare products Regulatory Agency (MHRA) or others, review and approve new medicines. These agencies may also be granted direct access to patients' information.
3. Trusted third parties working on behalf of GSK and/or institutions working with GSK who are contractually bound to protect your coded data.
The sponsor may share or provide access to data about patients outside the UK for research-related purposes.

IPD sharing plan summary
Other