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Study of intranasal cenegermin in adult participants with moderate to severe traumatic brain injury

Submission date
08/05/2026

Recruitment status
Recruiting

Registration date
27/11/2026

Overall study status
Ongoing

Last Edited
27/11/2026

Condition category
Nervous System Diseases

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
A moderate or severe traumatic brain injury (TBI) can cause long-term problems with thinking, memory, movement and emotions. There are currently no approved treatments that directly help the brain recover after this type of injury. This study is testing cenegermin, a nasal spray containing a laboratory-made version of nerve growth factor (NGF), a natural protein that helps protect brain cells and support their recovery. The study aims to evaluate the safety and tolerability of intranasal cenegermin in people with moderate to severe subacute TBI, assess whether it improves recovery compared with a vehicle nasal spray, evaluate long-term safety and tolerability, determine how the drug moves through the blood and cerebrospinal fluid, and assess whether it causes the body to produce antibodies against the treatment.

Who can participate?
Adults aged 18 to 70 years with moderate to severe traumatic brain injury who had a TBI resulting in hospital evaluation between 2 and 8 weeks before giving consent, have a confirmed TBI diagnosis requiring head CT imaging, and are currently undergoing rehabilitation or are expected to be discharged to a rehabilitation setting.

What does the study involve?
The study is divided into two parts. In Part A, participants who have experienced a moderate or severe TBI in the previous few weeks will be randomly assigned to receive either a high dose of cenegermin nasal spray, a low dose of cenegermin nasal spray, or a vehicle nasal spray that does not contain the active medicine. Independent experts on a Data Monitoring Committee will review safety data collected during this phase and decide whether one or both doses should continue into Part B.

In Part B, the study continues using the selected dose or doses until the planned number of participants has been enrolled.
Participants will receive study treatment according to the study schedule and will undergo safety assessments including clinical laboratory tests, physical examinations, vital signs measurements, electrocardiograms (ECGs), MRI scans, and monitoring of adverse events. Follow

up assessments may continue for up to 12 months after the first administration of the study treatment. Some participants may also take part in optional cerebrospinal fluid (CSF) sub-study.

What are the possible benefits and risks of participating?
Possible benefits include helping researchers determine whether cenegermin can improve recovery after moderate to severe traumatic brain injury. However, benefit to individual participants cannot be guaranteed.

Potential risks include adverse events associated with cenegermin, nasal administration and study procedures. Intranasal administration may cause burning, stinging, dryness, congestion, sneezing, coughing or nosebleeds. Blood tests may cause pain, bruising, irritation, redness, infection, faintness or dizziness. ECG pads may cause skin irritation or itching. Eye assessments may cause temporary dryness, fatigue, blurred vision, light sensitivity or fatigue during testing. MRI scans may cause feelings of claustrophobia.

Additional risks associated with the CSF sub-study may include complications of lumbar puncture, such as headache, infection, cerebrospinal fluid leakage or nerve injury, and exposure to radiation during X-ray procedures. Local anaesthetic use may cause injection-site reactions and, rarely, severe allergic reactions.

Where is the study run from?
The University of Edinburgh, UK.

When is the study starting and how long is it expected to run for?
October 2026 to December 2028.

Who is funding the study?
Dompé farmaceutici S.p.A, Italy.

Who is the main contact?
Emma Sheahan (Scientific/Public Contact), iconregulatoryaffairs@iconplc.com
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Additional identifiers

Integrated Research Application System (IRAS)
1013860

Sponsor's protocol code number
NGF-TBI-201

Study information

Scientific Title
Randomized, double-blinded, vehicle-controlled, parallel group, adaptive proof-of-concept, dose-selecting phase 2a study to evaluate the safety, tolerability, pharmacokinetics, pharmacodynamics and efficacy of intranasal cenegermin (recombinant human nerve growth factor [rhNGF]) in adult participants with subacute moderate to severe traumatic brain injury (TBI)

Study objectives
1. To evaluate the safety and tolerability of intranasal cenegermin in participants with moderate to severe subacute TBI.

1. To evaluate improvements in the global outcome of participants with moderate to severe subacute TBI following intranasal administration of cenegermin compared to vehicle.
2. To evaluate the long-term safety and tolerability of intranasal cenegermin in participants with moderate to severe subacute TBI.
3. To determine the systemic pharmacokinetic (PK) characteristics of intranasal cenegermin in participants with moderate to severe subacute TBI.
4. To determine the PK characteristics of intranasal cenegermin in cerebrospinal fluid (CSF) of participants with moderate to severe subacute TBI.
5. To assess the immunogenicity of intranasal cenegermin in participants with moderate to severe subacute TBI.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 04/09/2026, Scotland A Research Ethics Committee (South East Scotland Research Ethics Service, Mainpoint, 102 Westport, Edinburgh, EH3 9ND, United Kingdom; +44 (0)781 460 9032; loth.sesres@nhs.scot), ref: 26/SS/0051

Primary study design
Interventional

Allocation
Randomized controlled trial

Masking
Blinded (masking used)

Control
Placebo

Assignment
Parallel

Purpose
Safety

Study type(s)
Efficacy, Safety, Other

Health condition(s) or problem(s) studied
Subacute moderate to severe traumatic brain injury

Interventions
Participants were randomised using a computer generated method to the following arms:

Arm 1 (cenegermin 180 µg): Participants will receive 180 µg cenegermin on days 1 through 7 of each 28-day treatment cycle
Arm 2 (cenegermin 90 µg): Participants will receive 90 µg cenegermin on days 1 through 7 of each 28-day treatment cycle
Arm 3 (vehicle): Participants will receive vehicle on days 1 through 7 of each 28-day treatment cycle

Cenegermin and vehicle will be intranasally using a CE Marked device (MAD Nasal™; Teleflex Medical)

Intervention Type
Drug

Phase
Phase II

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

Primary outcome(s)
1. Incidence of treatment-emergent serious and non-serious adverse events through 6 months following the first intranasal administration of cenegermin, measured using data reported by the participant or care partner. The investigator and any qualified designees are responsible for detecting, documenting, and recording events that meet the definition of an adverse event or serious adverse event, with data collation at study end.

Key secondary outcome(s)
1. Global functional outcome measured using the Glasgow Outcome Scale-Extended (GOS-E), including the proportion of participants achieving a good functional outcome defined as an improvement of at least 2 GOS-E levels from baseline; at baseline and 6 months

2. Incidence of treatment-emergent serious and non-serious adverse events and treatment emergent adverse events of special interest through 6 months following the first intranasal administration of cenegermin, measured using data reported by the participant or care partner. The investigator and any qualified designees are responsible for detecting, documenting, and recording events that meet the definition of an adverse event or serious adverse event, with data collation at study end.

3. Participant incidence of study discontinuation for tolerability reasons measured using investigator-assessed adverse events leading to treatment discontinuation over 12 months from first intranasal administration of investigational product, determined at study end

4. Changes in safety assessments from baseline through 12 months following the first administration of investigational product measured using vital signs (blood pressure, heart rate, respiratory rate, and body temperature), 12-lead ECG results, clinical laboratory assessments,

general physical examinations including neurological, ocular, and ear, nose, and throat (ENT) evaluations, brain MRI (eg, T1, FLAIR, T2* sequences), and the Columbia Suicidality Severity Rating Scale (C-SSRS), with data collation at study end

5. Blood nerve growth factor (NGF) concentration measured using blood sample analysis at pre-dose and approximately 2 hours post-dose on Days 1 and 7 of Cycles 1 and 4

6. Cerebrospinal fluid (CSF) nerve growth factor (NGF) concentration measured using CSF sample analysis (CSF biomarker substudy only) at pre-dose on Day 1 of Cycles 1 and 4 and approximately 2 hours post-dose on Day 7 of Cycles 1 and 4

7. Anti-cenegermin anti-drug antibody (ADA) levels measured using blood sample analysis for anti-cenegermin binding and neutralising antibodies at baseline and 12 months from first intranasal administration of investigational product

Completion date
17/07/2028

Eligibility

Key inclusion criteria
1. Participant is capable and willing to provide informed consent OR their legally authorized representative (LAR) is willing to provide informed consent on behalf of the participant, should the participant lack decision-making capacity.
2. Participant has a designated care partner (eg, spouse, adult child) who is capable and willing to provide informed consent to participate in study-related assessments (eg, Zarit Burden Interview [ZBI]).
3. Male and female participants 18 to 70 years of age are eligible to participate, with the following caveats:
3.1. A female participant is eligible to participate if she is not pregnant or breastfeeding, and one of the following conditions applies:
3.1.1. Is a woman of non-childbearing potential
3.1.2. Is a woman of childbearing potential (WOCBP) and using an acceptable contraceptive method during the study treatment period (at a minimum of until 30 days after the last dose of investigational medicinal product). A WOBCP must have a negative highly sensitive pregnancy test (urine or serum as required by local regulations) at screening, confirmed by a negative urine pregnancy test at baseline prior to study treatment administration.
3.2. Male Participants are eligible to participate if they agree to the following during the study treatment period and for at least 30 days after the last dose of study treatment:
3.2.1. Refrain from donating fresh unwashed semen.
3.2.2. Agree to use a male condom when having sexual intercourse with a WOCBP.
4. TBI resulting in hospital evaluation ≥ 2 to ≤ 8 weeks prior to informed consent.
5. Moderate to Severe TBI defined by Glasgow Coma Scale (GCS) score of 3 to 12 (considering the highest GCS score assessed within 24 hours of injury).
6. Confirmed TBI diagnosis requiring imaging evaluation with head CT.
7. Currently undergoing rehabilitation, or anticipated discharge to a rehabilitation setting (either at an inpatient/outpatient facility or with ambulatory care at home).

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 Years

Upper age limit
70 Years

Sex
All

Total final enrolment
0

Key exclusion criteria
1. Glasgow Outcome Scale - Extended (GOS-E) scores of 7 (lower good recovery) or 8 (upper good recovery) at the time of informed consent.
2. Penetrating TBI (eg, gunshot, stabs).
3. Medically refractory brain edema at the time of screening.
4. Post TBI epilepsy.
5. Evidence of active CSF leak at screening.
6. Medical history prior to TBI event of underlying metabolic, cardiovascular, pulmonary comorbidities that are considered severe and unstable by investigator assessment.
7. Dependence on invasive mechanical ventilation without the ability to sustain spontaneous breathing at time of screening.
8. Liver function test abnormalities: aspartate aminotransferase (AST), alanine aminotransferase (ALT), or bilirubin > 3x upper limit of normal (ULN).
9. Has a positive HIV, hepatitis B, or hepatitis C screen test.
10. Renal impairment (glomerular filtration rate [GFR] < 35).
11. Pre-existing medical condition prior to TBI event that in the opinion of the investigator continues to produce functional disability up to the time of injury, including disabling developmental, neurologic, psychiatric, and medical disorders.
12. Medical history of disabling neurologic or neurodegenerative disorders (eg, Alzheimer’s disease, Parkinson's disease, Multiple Sclerosis, Amyotrophic Lateral Sclerosis, Huntington’s disease).
13. Participation in another interventional clinical trial within 30 days prior to screening, or planned participation in any other clinical trial during study treatment and follow-up.
14. Concomitant or planned use of systemic immunosuppressants (eg, anti-CD20 monoclonal antibodies, methotrexate) during the study.
15. Known active substance abuse or dependency, including but not limited to alcohol, illicit drugs, or misuse of prescription medications.
16. Known active malignancy, history of malignancy within the past 5 years in any organ system requiring oncological treatment (surgery, chemotherapy, immunotherapy, radiotherapy) except for basal cell carcinoma that has been surgically treated with confirmation of remission for at least 1 year, or history of CNS malignancy at any time point.
17. Clinical and/or radiological diagnosis of acute spinal cord injury with neurological deficit.
18. Conditions that preclude the effective delivery of the IMP to the cribriform plate, such as anatomical abnormalities detected by physical examination of the nose or imaging, face trauma preventing IMP delivery, fracture of the frontal maxillary and/or nasal region, and allergic rhinitis.
19. History of a serious adverse reaction or known significant hypersensitivity to any drug or

chemically related compounds to the IMP or its excipients.
20. Contraindications to magnetic resonance imaging (MRI) (eg, non-MRI compatible pacemaker or implantable cardioverter-defibrillator), or inability to undergo MRI (eg, due to a medical history of claustrophobia).

Participants are not eligible for inclusion in the CSF biomarker sub-study if any of the additional following criteria apply:
1. Contraindications to lumbar puncture (eg, platelet count < 100 x 109/L).
2. Presence of a ventriculoperitoneal shunt.
3. Requires consent from a LAR.
4. Lumbar puncture requiring X-ray or any other imaging guidance (Germany only).

Date of first enrolment
07/10/2026

Date of final enrolment
31/05/2028

Locations

Countries of recruitment
United Kingdom

England

Scotland

Wales

Denmark

Finland

France

Italy

Poland

Spain

Sweden

Study participating centre
St James' S University Hospital
Beckett Street
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Study participating centre
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Study participating centre
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Sponsor information

Organisation
Dompé (Italy)

ROR
https://ror.org/04erezm33

Funder(s)

Funder type

Funder Name
Dompé farmaceutici S.p.A, Italy

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated and/or analysed during the current study will be published as a supplement to the results publication

IPD sharing plan summary
Published as a supplement to the results publication