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A 2-part, randomized, double-blind, placebo-controlled study in participants with Duchenne muscular dystrophy amenable to exon 45 skipping to evaluate the safety and efficacy of ENTR-601-45 (ELEVATE-45)

Submission date
28/12/2024

Recruitment status
Not yet recruiting

Registration date
30/05/2025

Overall study status
Ongoing

Last Edited
01/07/2025

Condition category
Nervous System Diseases

[X] 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
The study aims to determine if ENTR-601-45 is safe, identify any side effects, and see how well it works on DMD by possibly increasing dystrophin protein production. Dystrophin helps muscles function properly. ENTR-601-45 is an investigational medication, meaning it has not been approved by the Medicines and Healthcare products Regulatory Agency (MHRA), the health authority that gives approval for new medications in the United Kingdom.

Who can participate?
This study is for ambulatory minors and adults aged 4 to 20 years old, inclusive, who were assigned male at birth, have a confirmed diagnosis of Duchenne muscular dystrophy, and have a genetic variant of the dystrophin gene that allows ENTR-601-45 to skip exon 45. People cannot take part if they have another ongoing disease or condition affecting the kidneys.

What does the study involve?
Participants will receive either ENTR-601-45 or a placebo (a substance with no active ingredients). At the end of the 25 weeks of the study, all participants (including those who received a placebo) may be able to receive ENTR-601-45 in a long-term study.
All participants will be screened to confirm eligibility for participation. This involves providing biological samples (e.g., blood and urine) and undergoing additional physical procedures at study visits. Participants will have two muscle biopsies over the course of the study. Muscle biopsies are important because they allow researchers to compare whether there have been changes in the muscle as a result of the study drug. The study requires regular health check visits, which will be completed according to a schedule. During these visits, various tests will be conducted, including physical exams, heart rate, temperature, blood pressure, electrocardiogram, echocardiogram, and muscle function tests.

What are the possible benefits and risks of participating?
Participants may or may not benefit from this study. Participation could help increase knowledge about DMD and the study medication. The possible benefit of receiving ENTR-601-45 for participants is dystrophin production may increase and improve muscle function, but there is no guarantee this will happen. This is the first study of ENTR-601-45 in humans; therefore, there is no previous information on possible benefit in humans.
Similarly, this is the first study with the medication in humans, there is no previous information on side effects in humans. There have been studies done in laboratories on animals, and there have been studies with similar medicines. From this research, possible side effects might include issues with kidney function, blood clotting, blood cell count, and liver enzymes. There could also be side effects from the medication administration and muscle biopsies. However, researchers do not know all the side effects that could happen.

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

When is the study starting and how long is it expected to run for?
December 2024 to March 2029

Who is funding the study?
The Sponsor, Entrada Therapeutics, Inc., is providing financial support and materials for this study. The study site is being paid by the Sponsor to do this study. Otherwise, the site staff including the study doctor have no financial ties to the Sponsor.

Who is the main contact?
clinicaltrials@entradatx.com

Contact information

Type(s)
Scientific

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Public, Scientific

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Additional identifiers

EudraCT/CTIS number
2024-517499-39

IRAS number
1010846

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
ENTR-601-45-201, CPMS 66105

Study information

Scientific Title
A 2-part, randomized, double-blind, placebo-controlled study in participants with Duchenne muscular dystrophy amenable to exon 45 skipping with an initial multiple ascending dose part A to assess the safety, tolerability, pharmacokinetics and pharmacodynamics of ENTR-601-45, followed by part B to evaluate the safety and efficacy of ENTR-601-45 (ELEVATE-45)

Acronym
ELEVATE-45

Study objectives
Key Objectives (Part A):
1. To evaluate the safety and tolerability of ENTR-601-45 in participants with Duchenne muscular

dystrophy (DMD)
2. To characterize the pharmacokinetics of ENTR-601-45 in participants with DMD
3. To characterize the pharmacodynamics of ENTR-601-45 in participants with DMD
4. To evaluate the immune response to ENTR-601-45 in participants with DMD

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 19/03/2025, London – Brent Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, UK; Tel: N/A; brent.rec@hra.nhs.uk), ref: 25/LO/0074

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

Primary study design
Interventional

Secondary study design
Randomised parallel trial

Study setting(s)
Hospital

Study type(s)
Safety, Efficacy

Participant information sheet
Not available in web format, please use the contact details to request a participant information sheet

Health condition(s) or problem(s) studied
Duchenne muscular dystrophy

Interventions
Experimental: ENTR-601-45.
Participants will receive a fixed number of doses at one of three dose levels. One dose will be given every 6 weeks.
Drug: ENTR601-45. Given by IV infusion as specified under Participant Group/Arm.

Placebo Comparator Arm: ENTR-601-45 matching placebo
Participants will receive a fixed number of placebo doses matched to ENTR-601-45 doses. One dose will be given every 6 weeks.
Drug: ENTR-601-45 – Matching Placebo: Given by IV infusion as specified under Participant Group /Arm.

Intervention Type
Drug

Pharmaceutical study type(s)
Pharmacokinetic, Pharmacodynamic, Dose response, Therapy

Phase
Phase I/II

Drug/device/biological/vaccine name(s)
ENTR-601-45

Primary outcome measure
1. Overall safety and tolerability of ENTR-601-45, measured using:
1.1. Incidence and severity of treatment-emergent adverse events (TEAEs)
1.2. Changes in vital sign measurements
1.3. Clinical laboratory results
1.4. Electrocardiogram (ECG) parameters
1.5. Physical examination findings
From baseline through the End of Study visit

Secondary outcome measures
1. Plasma, muscle, and urine concentration of ENTR-601-45 and its final metabolite at prespecified timepoints during the study
2. Change from baseline in dystrophin by Western blot from muscle biopsy at the End of Study
3. Change from baseline in dystrophin expression and localization from muscle biopsy at the End of Study
4. Percent change from baseline in exon 45 skipping measured in muscle biopsy at the End of Study
5. Anti-drug antibody (ADA) and anti-dystrophin antibody in serum at prespecified timepoints during the study

Overall study start date
23/12/2024

Completion date
01/03/2029

Eligibility

Key inclusion criteria
1. Genetic diagnosis of DMD and confirmed pathologic variant in the dystrophin gene amenable to exon 45 skipping as reviewed by a central genetic counselor
2. Assigned male at birth with clinical signs compatible with Duchenne muscular dystrophy as determined by the investigator
3. Part A: 4-20 years of age, inclusive
4. Ambulatory Status Part A: ambulatory with a Performance of the Upper Limb v2.0 (PUL 2.0) Entry as per protocol at Screening
5. Adequate muscle for obtaining tissue biopsy as assessed by the investigator
6. Other protocol-defined criteria apply

Participant type(s)
Patient

Age group

Mixed

Lower age limit
4 Years

Upper age limit
20 Years

Sex
Male

Target number of participants
24

Key exclusion criteria
1. Any significant concomitant medical condition that might interfere with the ability to comply with protocol requirements.
2. Has an acute illness within 4 weeks prior to the first dose of study drug which may interfere with study measurements or jeopardize the participant’s safety
3. Use of the following medications:
3.1. Prior treatment with any exon skipping therapy at any time
3.2. Prior or current treatment with any gene therapy at any time
3.3. Use of anti-coagulants, anti-thrombotics, or anti-platelet agents
3.4. Use of an immunosuppressant for a non-DMD condition from 30 days prior to screening until the end of the study
3.5. Has taken or is currently taking a histone deacetylase (HDAC) inhibitor, including (but not limited to) givinostat from at least 30 days
prior to the start of the screening period until the end of the study
4. Laboratory abnormalities
5. Daytime ventilator dependence or any use of invasive mechanical ventilation via tracheostomy
6. Has an abnormal electrocardiogram (ECG) reading assessed as clinically significant by the investigator, and/or a QT interval with Fridericia correction method (QTcF) >450 msec at Screening or prior to the first dose of study drug on Day 1
7. Received any experimental or investigational drug, etc within 3 months prior to first dose or within 5 half-lives (whichever is longer)
8. Other protocol-defined criteria apply

Date of first enrolment
30/09/2025

Date of final enrolment
03/08/2028

Locations

Countries of recruitment
Belgium

England

Italy

Netherlands

Spain

United Kingdom

Study participating centre
UZ Leuven
Belgium
-

Study participating centre
University Hospital Gent
Belgium
-

Study participating centre
Centre Hospitalier Régional de la Citadelle
Belgium
-

Study participating centre
IRCCS Ospedale San Raffaele
Italy
-

Study participating centre
Fondazione Policlinico Universitario A. Gemelli IRCCS - Universita Cattolica del Sacro Cuore
Italy
-

Study participating centre
Ospedale Pediatrico Bambino Gesu
Italy
-

Study participating centre
Hospital Sant Joan de Deu
Spain
-

Study participating centre
Hospital Universitario Vall d'Hebron
Spain
-

Study participating centre
Stichting Radboud Universitair Medisch Centrum
Netherlands
-

Study participating centre
Leids Universitair Medisch Centrum
Netherlands
-

Study participating centre
Great Ormond Street Hospital for Children
Great Ormond Street
London
United Kingdom
WC1N 3JH

Study participating centre
Alder Hey Children's NHS Foundation Trust
Alder Hey Hospital
Eaton Road
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Liverpool
United Kingdom
L12 2AP

Study participating centre

Leeds General Infirmary
Great George Street
Leeds
United Kingdom
LS1 3EX

Study participating centre
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M27 4HA

Study participating centre
Oxford University Hospitals NHS Foundation Trust
John Radcliffe Hospital
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Sponsor information

Organisation
Entrada Therapeutics, Inc.

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Sponsor type
Industry

Funder(s)

Funder type
Industry

Funder Name
Entrada Therapeutics

Alternative Name(s)
Entrada Therapeutics, Inc.

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
United States of America

Results and Publications

Publication and dissemination plan
1. Peer-reviewed scientific journals
2. Internal report
3. Conference presentation
4. Publication on website
5. Other publication
6. Submission to regulatory authorities

Study data will be posted as per local regulatory requirements, and all participant data will be pseudonymised through the use of a code (this is known as the participation identification number). Following completion of the study, the data may be considered for publication in a scientific journal or for reporting at a scientific meeting. Each Investigator is obligated to keep data pertaining to the study confidential. The Investigator must consult with the Sponsor and obtain approval before any study data is submitted for publication.

Intention to publish date
31/10/2029

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are not expected to be made available due to due to the data’s high commercial sensitivity.

IPD sharing plan summary
Not expected to be made available