ISRCTN15088415 https://doi.org/10.1186/ISRCTN15088415

A 2-part, randomized, double-blind, placebo-controlled study in participants with Duchenne muscular dystrophy amenable to exon 44 skipping to evaluate the safety and efficacy of ENTR-601-44 (ELEVATE-44)

Submission date
26/11/2024

Recruitment status
Recruiting

Registration date
12/05/2025

Overall study status
Ongoing

Last Edited
01/07/2025

Condition category
Genetic 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
This study aims to determine if ENTR-601-44 is safe, identify any side effects, and see how well it works on Duchenne muscular dystrophy (by increasing the amount of dystrophin protein that is produced). Dystrophin helps muscles function properly. ENTR-601-44 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 variant of the dystrophin gene that allows ENTR-601-44 to skip exon 44.

What does the study involve?
Participants will receive either ENTR-601-44 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 placebo) may be able to receive ENTR-601-44 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 2 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-601-44 for participants is dystrophin production may increase and improve muscle function, but there is no guarantee this will happen. This is an early study of ENTR-601-44 in individuals with DMD, and therefore information on its potential positive effects in people is limited.
Since this is an early study with the medication in humans, there is limited information on side effects. There have been studies done in laboratories on animals, there has been one other study on healthy men, 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?

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?

Study website
https://www.elevate44study.com

Contact information

Type(s)
Public, Scientific

Contact name
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Principal Investigator

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Additional identifiers

EudraCT/CTIS number
2024-517584-23

IRAS number
1010840

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
ENTR-601-44-201, CPMS 65821

Study information

Scientific Title
A 2-part, randomized, double-blind, placebo-controlled study in participants with Duchenne muscular dystrophy amenable to exon 44 skipping with an initial multiple ascending dose part A to assess the safety, tolerability, pharmacokinetics and pharmacodynamics of ENTR-601-44, followed by Part B to evaluate the safety and efficacy of ENTR-601-44 (ELEVATE-44)

Acronym
ELEVATE-44

Study objectives
Key Objectives (Part A)
1. To evaluate the safety and tolerability of ENTR-601-44 in participants with Duchenne muscular dystrophy (DMD)
2. To characterize the pharmacokinetics of ENTR-601-44 in participants with DMD
3. To characterize the pharmacodynamics of ENTR-601-44 in participants with DMD
4. To evaluate the immune response to ENTR-601-44 in participants with DMD

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 27/01/2025, South Central - Oxford A Research Ethics Committee (Ground Floor Temple Quay House 2 The Square, Bristol, BS1 6PN, United Kingdom; +44 207 104 8118; oxforda.rec@hra.nhs.uk), ref: 24/SC/0403

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
No participant information sheet available

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

Interventions
Part A
Experimental Arm: ENTR-601-44.
• Participants will receive a fixed number of doses at one of three dose levels. One dose will be given every six
weeks.
• Drug: ENTR-601-44: Given by IV infusion as specified under Participant Group/Arm.

Placebo Comparator Arm: ENTR-601-44 matching placebo
• Participants will receive a fixed number of placebo doses matched to ENTR-601-44 doses. One dose will be given every six weeks.
• Drug: ENTR-601-44 – 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-601-44

Primary outcome measure
Safety and tolerability of ENTR-601-44 measured using incidence and severity of treatment-emergent adverse events (TEAEs); changes in vital sign measurements, clinical laboratory results, electrocardiogram (ECG) parameters, physical examination findings from baseline through End of Study visit

Secondary outcome measures
1. Plasma, muscle, and urine concentration of ENTR-601-44 and its final metabolite at timepoints as specified in the study protocol
2. Change from baseline in dystrophin by Western blot from muscle biopsy at End of Study
3. Change from baseline in dystrophin expression and localization from muscle biopsy at End of Study
4. Percent change from baseline in exon 44 skipping measured in muscle biopsy at End of Study
5. Anti-drug antibody (ADA) and anti-dystrophin antibody in serum at Baseline, End of Study, and additional timepoints as specified in the study protocol

Overall study start date
22/11/2024

Completion date
28/03/2029

Eligibility

Key inclusion criteria
Principal inclusion criteria
1. Genetic diagnosis of DMD and confirmed pathologic variant in the dystrophin gene amenable to exon 44 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

Principal 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 participant’s safety.
3. Use of the following medications:
3.1. Prior treatment with any exon skipping therapy at any time
3.2. Prior treatment with any gene therapy at any time
3.3. Use of anti-coagulants, anti-thrombotics, or anti-platelet agents from at least 30 days prior to the start of the screening period until the end of the study
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
30/06/2025

Date of final enrolment
18/08/2028

Locations

Countries of recruitment
Belgium

Italy

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 Serena Onlus - Centro Clinico NeMO Milano
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
Great Ormond Street Hospital for Children
Great Ormond Street
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Study participating centre
Freeman Hospital
Freeman Road
High Heaton
Newcastle upon Tyne
United Kingdom
NE7 7DN

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

Study participating centre
Leeds General Infirmary
Great George Street
Leeds
United Kingdom
LS1 3EX

Study participating centre
Royal Manchester Childrens Hospital
Hospital Road
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Manchester

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Sponsor information

Organisation
Entrada Therapeutics, Inc.

Sponsor details
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Sponsor type
Industry

Funder(s)

Funder type
Industry

Funder Name
Entrada Therapeutics, Inc.

Results and Publications

Publication and dissemination plan
Peer reviewed scientific journals
Internal report
Conference presentation
Publication on website
Other publication
Submission to regulatory authorities
Study data will be posted as per local regulatory requirements, and all participant data will be pseudonymised through 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
30/09/2029

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, Data sharing statement to be made available at a later date