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Reporting Summary

Nature Research wishes to improve the reproducibility of the work that we publish. This form provides structure for consistency and transparency in reporting. For further information on Nature Research policies, see Authors & Referees and the Editorial Policy Checklist.

Statistical parameters

When statistical analyses are reported, confirm that the following items are present in the relevant location (e.g. figure legend, table legend, main text, or Methods section).

n/a	Confirmed	
☐	☒	The exact sample size (*n*) for each experimental group/condition, given as a discrete number and unit of measurement
☐	☒	An indication of whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
☐	☒	The statistical test(s) used AND whether they are one- or two-sided *Only common tests should be described solely by name; describe more complex techniques in the Methods section.*
☒	☐	A description of all covariates tested
☐	☒	A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons
☐	☒	A full description of the statistics including central tendency (e.g. means) or other basic estimates (e.g. regression coefficient) AND variation (e.g. standard deviation) or associated estimates of uncertainty (e.g. confidence intervals)
☐	☒	For null hypothesis testing, the test statistic (e.g. *F*, *t*, *r*) with confidence intervals, effect sizes, degrees of freedom and *P* value noted *Give P values as exact values whenever suitable.*
☒	☐	For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings
☒	☐	For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes
☒	☐	Estimates of effect sizes (e.g. Cohen's *d*, Pearson's *r*), indicating how they were calculated
☒	☐	Clearly defined error bars *State explicitly what error bars represent (e.g. SD, SE, CI)*

Our web collection on statistics for biologists may be useful.

Software and code

Policy information about availability of computer code

Data collection	N/A
Data analysis	GraphPad Prism 7, Heidelberg Eye Explorer version 1.7.1.0

For manuscripts utilizing custom algorithms or software that are central to the research but not yet described in published literature, software must be made available to editors/reviewers upon request. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Research guidelines for submitting code & software for further information.

Data

Policy information about availability of data

All manuscripts must include a data availability statement. This statement should provide the following information, where applicable:

- Accession codes, unique identifiers, or web links for publicly available datasets
- A list of figures that have associated raw data
- A description of any restrictions on data availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Field-specific reporting

Please select the best fit for your research. If you are not sure, read the appropriate sections before making your selection.

☒ Life sciences ☐ Behavioural & social sciences ☐ Ecological, evolutionary & environmental sciences

For a reference copy of the document with all sections, see nature.com/authors/policies/ReportingSummary-flat.pdf

Life sciences study design

All studies must disclose on these points even when the disclosure is negative.

Sample size	14 (initially 12 consisting of 6 low dose and 6 high dose, subsequently increased by 2 following complication and protocol amendment
Data exclusions	Primary end-point analysis based on all 14 participants, subgroup analysis of 12 also performed after excluding two with surgical complications
Replication	No replicate tests performed at clinical trial follow-up visits. Trends can be seen based on multiple measurements over time.
Randomization	Non-randomised: as a safety study, the eye with worse visual acuity was generally treated, except in L3, H4 and H6 (Fig.2)
Blinding	Blinding was not performed as per protocol as part of this phase 1/2 (open-label) safety study.

Reporting for specific materials, systems and methods

Materials & experimental systems

n/a	Involved in the study
☒	☐ Unique biological materials
☐	☒ Antibodies
☐	☒ Eukaryotic cell lines
☒	☐ Palaeontology
☐	☒ Animals and other organisms
☐	☒ Human research participants

Methods

n/a	Involved in the study
☒	☐ ChIP-seq
☒	☐ Flow cytometry
☒	☐ MRI-based neuroimaging

Antibodies

Antibodies used	Anti-CHM or REP1 antibody (HPA003231, Sigma-Aldrich, Gillingham, UK; 1:1000 dilution for immunohistochemistry)
Validation	Polyclonal anti-human CHM antibody produced in rabbit is developed and validated by the Human Protein Atlas (HPA) project (www.proteinatlas.org). Each antibody is tested by immunohistochemistry against hundreds of normal and disease tissues.

Eukaryotic cell lines

Policy information about cell lines

Cell line source(s)	HEK293
Authentication	Not authenticated
Mycoplasma contamination	Not tested for mycoplasma contamination
Commonly misidentified lines (See ICLAC register)	No commonly misidentified cell lines were used.

Animals and other organisms

Policy information about studies involving animals; ARRIVE guidelines recommended for reporting animal research

Laboratory animals	JAX™ mice strain: wild-type C57BL/6J, female, between 6 to 8 weeks old at the time when experiments were set up

Wild animals	The study did not involve wild animals
Field-collected samples	The study did not involve samples collected from the field

Human research participants

Policy information about studies involving human research participants

Population characteristics	14 male patients with genetically confirmed mutations in the CHM gene - see Supplementary Table S1 for demographic details and dose allocation
Recruitment	Choroideremia patients were referred from across England via the four main retinal genetics centers (Oxford, London, Southampton and Manchester) as part of a UK national research ethics committee approved multicentre phase 1/2 clinical trial (ClinicalTrials.gov: NCT01461213). As this was primarily a safety study (the first trial of AAV gene therapy for choroideremia), patients with advanced choroideremia were generally selected and the worse eye was generally treated with gene therapy (see Fig.2).