Safety and Proof-of-Concept (POC) Study With AMT-130 in Adults With Early Manifest Huntington's Disease

Status: RECRUITING

Eligibility Criteria

Age: 25 years to 65 years old

This study is NOT accepting healthy

Healthy Volunteers: volunteers

Inclusion Criteria:

* Able and willing to provide written informed consent prior to the study and study-related procedure * Participants 25 to 65 years of age of both sexes * Cohorts 1, 2, \& 3: Early manifest HD as defined by a UHDRS total functional capacity (TFC) score of 9 to 13 and EITHER a diagnostic confidence level (DCL) of 4 OR a DCL of 3 if the subject either meets the definition of multidimensional manifest HD (UHDRS question 80) or has cognitive symptoms * Cohort 3: Early manifest HD as defined by a UHDRS TFC score of ≥ 11 and EITHER a DCL of 4 or a DCL of 3 with either a positive "Yes" response to UHDRS Question 80 (multidimensional manifest diagnosis on motor, cognitive, behavioral, functional) or DSM5 criteria for cognitive disorder (Movement Disorder Society Task Force criteria). * HTT gene expansion testing with the presence of ≥40 CAG repeats * Striatal MRI volume requirements per hemisphere: * Cohorts 1, 2, \& 3: Putamen ≥2.5 cm\^3 (per side); Caudate ≥2.0 cm\^3 (per side) * Cohort 4: Putamen \<2.5 cm\^3 (on either side); Caudate \<2.0 cm\^3 (on either side) * All HD concomitant medications (addressing motor, behavioral, and cognitive symptoms) must be stable for 3 months prior to Screening with no change in clinical symptoms requiring change in medication prior to anticipated administration procedure * Able and willing to comply with all procedures and the study visit schedule as outlined in the protocol * All female participants of childbearing potential (FOCP) must have a negative serum pregnancy test at Screening, (and Visit 1A, as appropriate), a negative pregnancy urine dipstick at Baseline, and not be breastfeeding. All FOCPs and sexually mature males must be compliant with a highly effective birth control method.

Exclusion Criteria:

* Evidence of suicide risk * Receipt of an experimental agent within 60 days or five half-lives prior to Screening or anytime over the duration of this study. * Participation in an investigational trial or investigational paradigm (such as exercise/physical activity, cognitive therapy, brain stimulation) within 60 days prior to Screening or anytime over the duration of this study. * Presence of an implanted deep brain stimulation device, ventriculoperitoneal or other CSF shunt, or other implanted catheter * Any history of gene therapy, RNA or DNA targeted HD specific investigational agents, such as antisense oligonucleotides (ASOs), cell transplantation or any other experimental brain surgery. * Any contraindication to 3.0 Tesla MRI as per local guidelines * Brain and spinal pathology that may interfere with the surgical delivery of AMT-130 or represents a significant neurologic comorbid disorder * Any contraindication to lumbar puncture as per local guidelines * Malignancy within 5 years of Screening, except for basal or squamous cell carcinoma of the skin or carcinoma in situ of the cervix that has been successfully treated * Hospitalization for any major medical or surgical procedure involving general anesthesia within 12 weeks of Screening or planned during the study * Current or recurrent disease, (including pre-existing cardiovascular or pulmonary conditions) infection, or other significant concurrent medical condition or medications that could confound clinical and laboratory evaluations or could affect a participant's safety or their ability to undergo the neurosurgical procedure or comply with the procedures and study visit schedule * Known or suspected intolerance or hypersensitivity to the investigational product(s), closely-related compounds, or any of the stated ingredients * Any known allergy to gadoteridol (ProHance) * Screening laboratory values (as measured by the central laboratory): a. Alanine aminotransferase (ALT) \>2 × upper limit of normal (ULN) b. Aspartate aminotransferase (AST) \>2 × ULN c. Total bilirubin \>2 × ULN d. Alkaline phosphatase (ALP) \>2 × ULN e. Creatinine \>1.5 × ULN f. Platelet count \ <100,000/mm3g.Prothrombin time (PT) \>1.2 × ULN h. Partial thromboplastin time (PTT) \>1.2 × ULN * Known allergy, sensitivity, or other contraindication to medications in the immunosuppression regimen in this protocol. * Any participant with an active infection (e.g., coronavirus disease 2019 \[COVID-19\]) at Screening or at the time of treatment that requires medical intervention. Participants may rescreen, or if screened eligible and an open surgical slot is available, may receive treatment after recovery. * Cohort 4 ONLY: Inability to establish a safe trajectory to administer AMT-130 to the target structures, as assessed by neuroimaging.

Conditions & Interventions

Interventions:
GENETIC: intra-striatal rAAV5-miHTT, OTHER: Imitation (sham) surgery
Conditions:
Huntington's Disease
Keywords:
Gene therapy, AAV (adeno-associated virus), serotype 5 AAV (adeno-associated virus), serotype 5, Viral vector, miHTT, muHTT, Huntington's Disease (HD)

More Information

Contact(s): uniQure - medinfo@uniqure.com
Principal Investigator: Barrett, Matthew, James
Phase: PHASE1
IRB
Number: HM20015806
System ID: NCT04120493
