A Treatment Study of Mucopolysaccharidosis Type IIIB (MPS IIIB)

ClinicalTrials.gov Identifier: NCT02754076

Recruitment Status : Completed
First Posted : April 28, 2016
Last Update Posted : August 6, 2020

Sponsor:
Allievex Corporation

Information provided by (Responsible Party):
Allievex Corporation

Study Description

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Brief Summary:
The study's primary objectives are to evaluate the safety and tolerability of AX 250 administered to subjects with MPS IIIB via an ICV reservoir and catheter and to evaluate the impact of AX 250 on cognitive function in patients with MPS IIIB as assessed by the Development Quotient.

Condition or disease	Intervention/treatment	Phase
MPS III B Mucopolysaccharidosis Type IIIB	Drug: AX 250	Phase 1 Phase 2

Study Design

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Study Type :
Interventional (Clinical Trial)

Actual Enrollment :
23 participants

Allocation:
N/A

Intervention Model:
Single Group Assignment

Masking:
None (Open Label)

Primary Purpose:
Treatment

Official Title:
A Phase 1/2 Open-Label Dose-Escalation Study to Evaluate the Safety, Tolerability, Pharmacokinetics and Efficacy of Intracerebroventricular AX 250 in Patients With Mucopolysaccharidosis Type IIIB (MPS IIIB, Sanfilippo Syndrome Type B)

Actual Study Start Date :
April 2016

Actual Primary Completion Date :
June 24, 2020

Actual Study Completion Date :
July 31, 2020

Resource links provided by the National Library of Medicine

MedlinePlus Genetics related topics: Mucopolysaccharidosis type III

Genetic and Rare Diseases Information Center resources: Mucopolysaccharidosis Mucopolysaccharidosis Type IIIB Mucopolysaccharidosis Type III Mucopolysaccharidosis Type IIIA

U.S. FDA Resources

Arms and Interventions

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Arm	Intervention/treatment
Experimental: AX 250 In Part 1, patients will receive up to 3 escalating doses of AX 250 (30, 100 and 300 mg) via ICV infusion every week until the maximum tolerated tested dose (MTTD) is established. In Part 2, patients will receive weekly doses of AX 250 via ICV infusion that will continue for 48 weeks at the MTTD established in Part 1.	Drug: AX 250 Chimeric fusion of recombinant human alpha-N-acetylglucosaminidase and truncated human insulin-like growth factor 2 (rhNAGLU-IGF2)

Outcome Measures

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Primary Outcome Measures :

1. Safety Evaluation of weekly infusions of AX 250 (Part 1 & Part 2) - Number of participants with abnormal clinical laboratory values and/or Adverse Events that are related to treatment.
   [Time Frame: Entire study period, up to 124 weeks]

   Number of participants with abnormal clinical laboratory values and/or Adverse Events that are related to treatment.

2. Development Quotient (DQ) as efficacy variable with analysis of rate of change of DQ score on treatment vs. rate of change of DQ score prior to treatment. [Time Frame: Assessed at study end, up to 124 weeks. Collected at: Part 1 - Baseline; Part 2 - Weeks 12, 24, 36, & 48]

Secondary Outcome Measures :

1. Characterize maximum concentration (Cmax) of AX 250 in cerebrospinal fluid (CSF) and plasma as relevant through completion of Part 1 and Part 2 [Time Frame: Study end, up to 124 weeks. Collected at: Pre-dose, 0, 4, 10, 24, 48, 72, 96, 168 hours post-dose for the first dose during each dose escalation in Part 1. Pre-dose, 0, 4, 10, 24, 48, 72, 96, 168 hours post-dose for Baseline, Weeks 5, 12, 36 in Part 2.]
2. Characterize area under concentration curve (AUC) of AX 250 in cerebrospinal fluid (CSF) and plasma as relevant through completion of Part 1 and Part 2 [Time Frame: Study end, up to 124 weeks. Collected at: Pre-dose, 0, 4, 10, 24, 48, 72, 96, 168 hours post-dose for the first dose during

each dose escalation in Part 1. Pre-dose, 0, 4, 10, 24, 48, 72, 96, 168 hours post-dose for Baseline, Weeks 5, 12, 36 in Part 2.]

3. Characterize immunogenicity of AX 250 total anti-drug anti-body (TAb) in cerebrospinal fluid (CSF) and serum as relevant through completion of Part 1 and Part 2 [Time Frame: Assessed at study end, up to 124 weeks. Collected at: First dose during each dose escalation in Part 1, and Weeks 0, 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48 in Part 2]
4. Evaluate GAG levels in cerebrospinal fluid (CSF) [Time Frame: Assessed at study end, up to 124 weeks. Collected at: Each weekly visit as relevant through completion of Part 1 and Part 2]
5. Evaluate GAG levels in plasma [Time Frame: Assessed at study end, up to 124 weeks. Collected at: Each weekly visit as relevant through completion of Part 1 and Weeks 0, 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48, as relevant in Part 2]
6. Evaluate GAG levels in urine [Time Frame: Assessed at study end, up to 124 weeks. Collected at: Each weekly visit as relevant through completion of Part 1 and Weeks 0, 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48, as relevant in Part 2]
7. Evaluate the impact of AX 250 treatment on brain structure assessed by magnetic resonance imaging (MRI) [Time Frame: Assessed at study end, up to 124 weeks. Part 1 - Screening and Baseline; Part 2 - Screening, Baseline, Week 24, and Week 48]

Eligibility Criteria

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Information from the National Library of Medicine

Choosing to participate in a study is an important personal decision. Talk with your doctor and family members or friends about deciding to join a study. To learn more about this study, you or your doctor may contact the study research staff using the contacts provided below. For general information, Learn About Clinical Studies.

Ages Eligible for Study:

1 Year to 10 Years (Child)

Sexes Eligible for Study:

All

Accepts Healthy Volunteers:

No

Criteria

Inclusion Criteria:

Individuals eligible to participate in Part 1 of this study must meet all of the following criteria:

- Has deficient NAGLU enzyme activity at Screening. Blood for NAGLU enzyme activity will be collected and analyzed centrally.
- Is ≥ 1 and < 11 years of age (at least 1 of the 3 subjects in Part 1 must be ≥ 1 and < 6 years of age)
- Has presented with signs/symptoms consistent with MPS IIIB; for individuals who have not presented with signs/symptoms of disease (eg, siblings of known patients), the determination of eligibility will be at the discretion of the BioMarin medical monitor in conjunction with the site investigator.
- Written informed consent from parent or legal guardian and assent from subject, if required
- Has the ability to comply with protocol requirements, in the opinion of the investigator

Individuals eligible to participate in Part 2 of this study must meet all of the following criteria:

- Participated in and met protocol requirements for transitioning from Study 250-901 or participated in Part 1 of Study 250-201
- Written informed consent from parent or legal guardian and assent from subject, if required

Exclusion Criteria:

Individuals who meet any of the following exclusion criteria are ineligible to participate in Part 1 of the study:

- Has received stem cell, gene therapy or ERT for MPS IIIB
- Has contraindications for neurosurgery (eg, congenital heart disease, severe respiratory impairment, or clotting abnormalities)
- Has contraindications for MRI scans (eg, cardiac pacemaker, metal fragment or chip in the eye, or aneurysm clip in the brain)
- Has a history of poorly controlled seizure disorder
- Is prone to complications from intraventricular drug administration, including patients with hydrocephalus or ventricular shunts
- Has received any investigational medication within 30 days prior to the Baseline visit or is scheduled to receive any investigational drug during the course of the study
- Has a medical condition or extenuating circumstance that, in the opinion of the investigator, might compromise the subject's ability to comply with protocol requirements, the subject's well-being or safety, or the interpretability of the subject's clinical data.
- Is pregnant at any time during the study

Individuals who meet any of the following exclusion criteria are ineligible to participate in Part 2 of this study:

- Has received stem cell, gene therapy or ERT for MPS IIIB
- Has contraindications for neurosurgery (eg, congenital heart disease, severe respiratory impairment, or clotting abnormalities)

- Has contraindications for MRI scans (eg, cardiac pacemaker, metal fragment or chip in the eye, or aneurysm clip in the brain)
- Is prone to complications from intraventricular drug administration, including patients with hydrocephalus or ventricular shunts
- Has received any investigational medication within 30 days prior to the Baseline visit or is scheduled to receive any investigational drug during the course of the study
- Has a medical condition or extenuating circumstance that, in the opinion of the investigator, might compromise the subject's ability to comply with protocol requirements, the subject's well-being or safety, or the interpretability of the subject's clinical data.
- Is pregnant at any time during the study

Contacts and Locations

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Information from the National Library of Medicine

To learn more about this study, you or your doctor may contact the study research staff using the contact information provided by the sponsor.

Please refer to this study by its ClinicalTrials.gov identifier (NCT number): ***NCT02754076***

Locations

United States, California

Children's Hospital Oakland
Oakland, California, United States, 94609

Colombia

Fundación Cardio Infantil - Instituto de Cardiología
Bogotá, Colombia

Germany

University Medical Center Hamburg Eppendorf, Department of Pediatrics
Hamburg, Germany

Spain

Hospital Clinico Universitario de Santiago
Santiago de Compostela, Spain

Taiwan

Mackay Memorial Hospital
Taipei, Taiwan, 10449

Turkey

Gazi Üniversitesi Tıp Fakültesi
Ankara, Turkey

United Kingdom

Somers Clinical Research Facility, Great Ormond Street Hospital
London, United Kingdom

Sponsors and Collaborators

Allievex Corporation

Investigators

Study Director: Allievex Medical Monitor Allievex Corporation

More Information

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Responsible Party:
Allievex Corporation

ClinicalTrials.gov Identifier:
NCT02754076 History of Changes

Other Study ID Numbers:
250-201

First Posted:
April 28, 2016 Key Record Dates

Last Update Posted:
August 6, 2020

Last Verified:
August 2020

Individual Participant Data (IPD) Sharing Statement:

Plan to Share IPD:
No

Keywords provided by Allievex Corporation:
Sanfilippo Syndrome Type B

Additional relevant MeSH terms:

Mucopolysaccharidoses

Mucopolysaccharidosis III

Carbohydrate Metabolism, Inborn Errors

Metabolism, Inborn Errors

Genetic Diseases, Inborn

Lysosomal Storage Diseases

Mucinoses

Connective Tissue Diseases

Metabolic Diseases