A Study of DB-OTO, an Adeno-Associated Virus (AAV) Based Gene Therapy, in Children/Infants, Adolescents and Adults With Hearing Loss Due to Otoferlin Mutations

Status: RECRUITING

Eligibility Criteria

Sex: ALL
Age:
Healthy Volunteers: This study is NOT accepting healthy volunteers
Key Inclusion Criteria:

1. Willingness to provide written informed consent (by at least one parent/legal guardian for pediatric participants, and with participant to provide assent, when applicable, or by the adult participant) and willingness to comply with trial protocol
2. Willingness to consent to genetic testing for the participant (by at least one parent/legal guardian for pediatric participants, and with participant to provide assent, when applicable, or by the adult participant) in order to evaluate a panel of hearing loss-related genes
3. Willingness to consent to vaccinations for the participant (by at least one parent/legal guardian for pediatric participants, and with participant to provide assent, when applicable, or by the adult participant) in accordance with the country-specific, age-appropriate immunization schedule, as described in the protocol
4. Participant able to perform all necessary assessments to qualify for enrollment and dosing in the corresponding cohort at the time the participant or parent/legal guardian signing the informed consent form (and participant providing assent, when applicable)
5. Presence of biallelic, likely pathogenic or pathogenic OTOF variants
6. No clinically significant laboratory findings on clinical laboratory tests at time of Screening as described in the protocol
7. Audiological Criteria:
    1. Investigator diagnoses the participant with profound sensorineural hearing loss (SNHL; >90 dB HL) based on behavioral and physiologic measurements (ABR) of inner ear function
    2. Outer hair cell presence is confirmed via presence of otoacoustic emissions (≥6 dBSNR) at ≥3 frequencies from 1 to 8 kHz in the ear(s) to be infused with DB-OTO. Alternatively, for participants >24 months of age, outer hair cell presence can be confirmed via presence of the cochlear microphonic in the ear(s) to be infused with DB-OTO.
8. No evidence from measures of hearing loss that show a dependence on body temperature
9. From study start and for the duration of the short-term follow-up period (48 weeks): Female participants of childbearing potential and fertile males, must agree to use highly effective contraception. Female participants must agree not to become pregnant. Fertile male participants must agree not to father a child or donate sperm, for 48 weeks and in cases of early withdrawal, for at least 12 months after DB-OTO administration.

Key Exclusion Criteria:

1. History of prior treatment with gene therapy
2. Surgical anatomy that would preclude or meaningfully impact the planned surgical approach as indicated by medical imaging (eg, Computed Tomography [CT] or Magnetic Resonance Imaging [MRI]) in the ear(s) to be infused with DB-OTO
3. History or presence of other permanent or untreatable hearing loss conditions
4. Prior or current history of malignancies
5. Prior or current history of meningitis
6. History or presence of cochlear implants in the ear(s) to be infused with DB-OTO
7. History of risk factor(s) for auditory neuropathy not caused by OTOF pathogenic variants including but not limited to: prematurity, low birth weight, hyperbilirubinemia, Neonatal Intensive Care Unit (NICU) admission, and/or low Apgar scores as described in the protocol

Note: Other protocol-defined inclusion/exclusion criteria apply

Conditions & Interventions

Interventions:
GENETIC: DB-OTO
Conditions:
Congenital Hearing Loss Secondary to Biallelic Mutations of the Otoferlin Gene (OTOF)
Keywords:
DB-OTO, Gene Therapy, Congenital Hearing Loss, Sensorineural Hearing Loss, Auditory Neuropathy, Pediatric, Cochlear Implant, Otoferlin, Deaf, Hard of hearing, Hearing impaired, Hearing disorder, Fully implantable hearing aid, Child, Infant, Adolescents, Young Adults, Adults, CHORD

More Information

Description:
Regeneron is conducting a study of an investigational new drug called DB-OTO. DB-OTO is a gene therapy that is being developed to treat pediatric and adult participants who have severe-to profound and profound hearing loss due to changes in the otoferlin gene. The purpose of this study is to: * Learn about the safety of DB-OTO * Determine how well DB-OTO is tolerated (does not cause ongoing discomfort) * Evaluate the efficacy of DB-OTO (how well DB-OTO works)

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