COMPASS

DENALI THERAPEUTICS

Information for Families

This brochure is an overview of the COMPASS study, including answers to frequently asked questions. The COMPASS study is a Phase 2/3 clinical study of DNL310, an investigational treatment for Hunter syndrome, also known as mucopolysaccharidosis type II (MPS II).

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Study Overview

- The COMPASS study will look at the potential impact of DNL310 on the behavioral, cognitive and physical components of MPS II compared with standard of care enzyme replacement therapy (ERT)
- The COMPASS study plans to enroll 54 participants globally including the United States, Europe, Latin America, and other global sites
- All participants will receive weekly intravenous (IV) infusions
- Participants are randomized 2:1, which means for every two children who receive DNL310, one child will receive standard of care
- This study is double-blinded; the doctors, study team, family, and participant will not know which children are assigned to which treatment. This helps to ensure and maintain the integrity of the study

Who can take part in this study?

Cohort A - Children who have a confirmed diagnosis of **neuronopathic** MPS II:	**Cohort B -** Children who have a confirmed diagnosis of **non-neuronopathic** MPS II:
• Are at least 2 years old but less than 6 years old	• Are at least 6 years old but less than 17 years old
Additional criteria may be required	

There are also criteria that would make your child unable to participate in the COMPASS study. For example, if they:

- Have a diagnosis other than MPS II that accounts for developmental delay
- Previously received an iduronate 2-sulfatase (IDS) gene therapy or stem cell therapy
- Received any central nervous system-targeted MPS ERT in the last 6 months
- Can't undergo lumbar punctures and/or MRIs
- Took part in any other investigational drug study, used an investigational drug within the last 60 days, or intend to receive another investigational drug during the study

Please contact a study doctor and discuss whether your child might be eligible.

Study Endpoints

Endpoints are the outcomes, or results, that will be measured in a clinical trial to objectively evaluate the safety and efficacy of treatment.

Primary endpoints:

- Reduction of heparan sulfate (HS) in the cerebrospinal fluid (CSF) (Cohort A)
- Change in the Vineland-3 Adaptive Behavior Scale (Cohort A)

Secondary endpoints:

- Changes in the Bayley Scales of Infant and Toddler Development (BSID) (Cohort A)
- Changes in the Six-Minute Walk Test (Cohort B)
- Changes in urine HS and dermatan sulfate (DS) concentrations (Cohorts A and B)
- Liver volume as measured by magnetic resonance imaging (MRI) (Cohorts A and B)
- Spleen volume as measured by MRI (Cohorts A and B)
- Improvement in Parent/Caregiver Global Impression of Change (CaGI-C) (Cohorts A and B)

Did you know?

The **Bayley Scales of Infant and Toddler Development** (BSID) is a set of task-based tests administered to the child that measure cognitive development.

The **Vineland-3 Adaptive Behavior Scale** is a tool administered to caregivers that measures how well children do everyday activities, such as communication, daily living skills, and socialization.

The **Parent/Caregiver Global Impression of Change (CaGI-C)** is a survey that a parent or caregiver completes to help clinicians assess improvement and impact of treatment.

COMPASS Study Timeline

Cohort A	Treatment Period (96 weeks)
Cohort B	Treatment Period (48 weeks)

Taking part in any Denali study is completely voluntary; individuals and children that participate may decide to leave at any time and can request guidance from the study team on how to do so safely.

Visit ClinicalTrials.gov **(study identifier: NCT05371613)** or clinicaltrialsregister.eu **(EudraCT Number: 2021-005200-35)** for additional information on this study.

DNL310 is an investigational drug and is not approved by any Health Authority, such as the U.S. Food and Drug Administration (FDA) or the European Medicines Agency (EMA).

Frequently Asked Questions

1. What is DNL310?

DNL310 is an investigational enzyme replacement therapy (ERT) for individuals with Hunter syndrome (MPS II). It is designed to utilize Denali's Transport Vehicle technology to deliver the needed enzyme (IDS) broadly throughout the body and brain through IV administration. By delivering medicine across the BBB, DNL310 aims to target the neurological symptoms of MPS II such as developmental delay, disruptive behaviors, and impaired cognition while also addressing the physical symptoms.

2. Why is crossing the blood-brain barrier important?

The human brain contains over 400 miles of blood vessels. These blood vessels are lined by closely linked cells to form the blood-brain barrier (BBB), which protects the brain from harmful elements. Many medicines can't reach the brain to treat neurocognitive symptoms because they are blocked by the BBB. DNL310 is uniquely designed to bind to the many Transferrin Receptors (TfRs) found at the BBB, enabling the needed enzyme to cross it. TfRs naturally carry iron across the BBB to the brain and may also help enzyme delivery into tissues throughout the body such as bone, cartilage, and the heart.

3. What is enzyme replacement therapy (ERT)?

ERT is designed to replace an enzyme that the body does not have enough of or is missing. While ERT does not cure lysosomal disorders, it does slow disease progression by increasing the amount of the missing enzyme in the body. MPS II and other lysosomal storage disorders typically require regular, lifelong ERT. Currently approved ERT does not cross the BBB to reach the brain resulting in the inability to adequately treat developmental symptoms.

4. Why is randomization needed for a study like the COMPASS study?

Randomization helps assess how effective a treatment may be by minimizing potential biases that could occur. These biases may influence the results of a clinical trial which can compromise the integrity of the study.

5. Where are the study sites located?

The COMPASS study will have sites in the United States, Europe, Latin America, and other global locations to be announced at a later date. **To learn more about COMPASS study sites, visit ClinicalTrials.gov and enter the study identifier: NCT05371613 or search for DNL310.**

All currently enrolling study sites are listed in the 'Contacts and Locations' section of the ***ClinicalTrials.gov*** website and sites will be added to this list as they begin actively enrolling. European residents can visit ***clinicaltrialsregister.eu*** for trial site information.

6. How is participation eligibility determined?

Eligibility is determined by the doctors at each study site. Contact your child's doctor and the clinical trial site contact for more information about the COMPASS study.

*For more information about the DNL310 clinical studies, please visit **ClinicalTrials.gov, clinicaltrialsregister.eu,** or speak with your child's doctor. Contact our patient advocacy team at **patients@dnli.com.***