MHRA
10 South Colonnade
Canary Wharf
London
E14 4PU
United Kingdom

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Decision Cover Letter

Decision of the licensing authority to:

agree a paediatric investigation plan

MHRA-100721-PIP01-22

Scope of the Application

Active Substance(s)

Recombinant fusion protein linking iduronate 2-sulfatase to engineered Fc with binding site for transferrin receptor (DNL310)

Condition(s)

Treatment of mucopolysaccharidosis II (Hunter syndrome)

Pharmaceutical Form(s)

Powder for concentrate for solution for infusion

Route(s) of Administration

INTRAVENOUS USE

Name / Corporate name of the PIP applicant

Denali Therapeutics Inc.

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, Denali Therapeutics Inc. submitted to the licensing authority on 17/11/2022 10:00 GMT an application for a Paediatric Investigation Plan

The procedure started on 12/04/2023 17:07 BST

1. The licensing authority, having assessed the application in accordance with the Human Medicines Regulations 2012, decides, as set out in the appended summary report:

to agree a paediatric investigation plan

2. The measures and timelines of the paediatric investigation plan are set out in the Annex I.

This decision is forwarded to the applicant, together with its annex and appendix.

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Final Decision Letter

MHRA-100721-PIP01-22

Of 24/05/2023 16:10 BST

On the adopted decision for Recombinant fusion protein linking iduronate 2-sulfatase to engineered Fc with binding site for transferrin receptor (DNL310) (MHRA-100721-PIP01-22) in accordance with the Human Medicines Regulations 2012.

The licensing authority, in accordance with the Human Medicines Regulations 2012, has adopted this decision:

Agreement on a paediatric investigation plan

This decision applies to a Paediatric Investigation Plan for Recombinant fusion protein linking iduronate 2-sulfatase to engineered Fc with binding site for transferrin receptor (DNL310), Powder for concentrate for solution for infusion , INTRAVENOUS USE .

This decision is addressed to Denali Therapeutics Inc., 161 Oyster Point Blvd., South San Francisco, UNITED STATES OF AMERICA, 94080

ANNEX I

1. Waiver

1.1 Condition:

Not applicable

2. Paediatric Investigation Plan:

2.1 Condition(s):

Treatment of mucopolysaccharidosis II (Hunter syndrome)

2.2 Indication(s) targeted by the PIP:

Treatment of mucopolysaccharidosis II (Hunter syndrome)

2.3 Subset(s) of the paediatric population concerned by the paediatric development:

The paediatric population from birth to less than 18 years of age

2.4 Pharmaceutical Form(s):

Powder for concentrate for solution for infusion

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	0	Not applicable.
Non-Clinical Studies	0	Not applicable.
Clinical Studies	3	Study 1 (DNLI-E-0002) Open-label study to evaluate safety, tolerability, pharmacokinetics (PK), pharmacodynamics (PD) and to explore the potential clinical efficacy of DNL310 in paediatric male patients from birth to less than 18 years of age (and adults) with mucopolysaccharidosis type II (MPS II; Hunter syndrome). Study 2 (DNLI-E-0007) Double-blind, randomised, two-arm study to evaluate the efficacy and safety of DNL310 versus idursulfase in paediatric participants from 2 years to less than 17 years of age with neuronopathic or non-neuronopathic MPS II. Study 3 (DNLI-E-0001) Prospective observational study of patients with MPS II to evaluate biomarkers potentially related to disease severity and/or treatment response and prospectively assess the progression of disease in patients from 2 years to less than 18 years of age (and adults) with MPS II.
Extrapolation, Modeling & Simulation Studies	0	Not applicable.
Other Studies	0	Not applicable.
Other Measures	0	Not applicable.

3. Follow-up, completion and deferral of a PIP:

Concerns on potential long term safety and efficacy issues in relation to paediatric use:	No
Date of completion of the paediatric investigation plan:	31/10/2025
Deferral of one or more studies contained in the paediatric investigation plan:	No