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

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Decision Cover Letter

Decision of the licensing authority to:

accept change(s) to the agreed paediatric investigation plan (MHRA-100721-PIP01-22)

MHRA-100721-PIP01-22-M01

Scope of the Application

Active Substance(s)

Tividenofusp alfa

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 20/02/2026 13:04 GMT an application for a Modification

The procedure started on 03/03/2026 18:13 GMT

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 accept change(s) to the agreed 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-M01

Of 15/06/2026 15:54 BST

On the adopted decision for Tividenofusp alfa (MHRA-100721-PIP01-22-M01) 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 modification of a paediatric investigation plan (including modification of a waiver or deferral included in that paediatric investigation plan)

This decision applies to a Modification for Tividenofusp alfa, 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 18 years of age (and young adults) 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:	31/12/2027
Deferral of one or more studies contained in the paediatric investigation plan:	No