EMA/826865/2022

European Medicines Agency decision

P/0429/2022

of 28 October 2022

on the agreement of a paediatric investigation plan for recombinant fusion protein linking iduronate 2-sulfatase to engineered Fc with binding site for transferrin receptor (DNL310) (EMEA-002845-PIP01-20) in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council

Disclaimer

This decision does not constitute entitlement to the rewards and incentives referred to in Title V of Regulation (EC) No 1901/2006.

Only the English text is authentic.

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The European Medicines Agency,

Having regard to the Treaty on the Functioning of the European Union,

Having regard to Regulation (EC) No 1901/2006 of the European Parliament and of the Council of 12 December 2006 on medicinal products for paediatric use and amending Regulation (EEC) No. 1768/92, Directive 2001/20/EC, Directive 2001/83/EC and Regulation (EC) No 726/2004[1],

Having regard to Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Union procedures for the authorisation and supervision of medicinal products for human use and establishing a European Medicines Agency[2],

Having regard to the application submitted by Denali Therapeutics Inc. on 9 July 2020 under Article 16(1) of Regulation (EC) No 1901/2006 also requesting a deferral under Article 20 of said Regulation and a waiver under Article 13 of said Regulation,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 9 September 2022, in accordance with Article 17 of Regulation (EC) No 1901/2006,

Having regard to Article 25 of Regulation (EC) No 1901/2006,

Whereas:

(1) The Paediatric Committee of the European Medicines Agency has given an opinion on the agreement of a paediatric investigation plan.

(2) It is therefore appropriate to adopt a decision agreeing a paediatric investigation plan.

[1] OJ L 378, 27.12.2006, p.1, as amended.
[2] OJ L 136, 30.4.2004, p. 1, as amended.

Has adopted this decision:

Article 1

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, the details of which are set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices, is hereby agreed.

Article 2

This decision is addressed to Denali Therapeutics Inc., 161 Oyster Point Blvd., 94080 - South San Francisco, CA, United States.

EMA/PDCO/573042/2022
Amsterdam, 9 September 2022

Opinion of the Paediatric Committee on the agreement of a Paediatric Investigation Plan

EMEA-002845-PIP01-20

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 opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, Denali Therapeutics Inc. submitted for agreement to the European Medicines Agency on 9 July 2020 an application for a paediatric investigation plan for the above mentioned medicinal product and a deferral under Article 20 of said Regulation and a waiver under Article 13 of said Regulation.

The procedure started on 18 August 2020.

Supplementary information was provided by the applicant on 24 May 2022. The applicant proposed modifications to the paediatric investigation plan and withdrew its request for a deferral and a waiver.

Opinion

1. The Paediatric Committee, having assessed the proposed paediatric investigation plan in accordance with Article 17 of Regulation (EC) No 1901/2006 as amended, recommends as set out in the appended summary report:

   - to agree the paediatric investigation plan in accordance with Article 17(1) of said Regulation.

   The Paediatric Committee member of Norway agrees with the above-mentioned recommendation of the Paediatric Committee.

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

This opinion is forwarded to the applicant and the Executive Director of the European Medicines Agency, together with its annex and appendix.

Annex I

The subset(s) of the paediatric population and condition(s) covered by the waiver and the measures and timelines of the agreed paediatric investigation plan (PIP)

1. Waiver

Not applicable

2. Paediatric investigation plan

2.1. Condition:

Treatment of mucopolysaccharidosis II (Hunter syndrome)

2.1.1. Indication(s) targeted by the PIP

Treatment of mucopolysaccharidosis II (Hunter syndrome)

2.1.2. Subset(s) of the paediatric population concerned by the paediatric development

From birth to less than 18 years of age.

2.1.3. Pharmaceutical form(s)

Powder for concentrate for solution for infusion

2.1.4. Measures

Area	**Description**
Quality-related studies	Not applicable.
Non-clinical studies	Not applicable.
Clinical studies	Study 1 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). (DNLI-E-0002) Study 2 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. (DNLI-E-0007) Study 3 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. (DNLI-E-0001)

Extrapolation, modelling and simulation studies	Not applicable.
Other studies	Not applicable.
Other measures	Not applicable.

3. Follow-up, completion and deferral of PIP

Concerns on potential long term safety/efficacy issues in relation to paediatric use:	No
Date of completion of the paediatric investigation plan:	By October 2025
Deferral for one or more measures contained in the paediatric investigation plan:	No