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

gov.uk/mhra

Decision Cover Letter

Decision of the licensing authority to:

agree a paediatric investigation plan and grant a deferral and grant a waiver

MHRA-101740-PIP01-24

Scope of the Application

Active Substance(s)

messenger RNA encoding Cas9; single guide RNA targeting the human KLKB1 gene

Condition(s)

Treatment of hereditary angioedema (HAE)

Pharmaceutical Form(s)

Dispersion for infusion

Route(s) of Administration

INTRAVENOUS USE

Name / Corporate name of the PIP applicant

Intellia Therapeutics, Inc.

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, Intellia Therapeutics, Inc. submitted to the licensing authority on 17/01/2025 14:13 GMT an application for a Paediatric Investigation Plan

The procedure started on 17/02/2025 17:47 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 agree a paediatric investigation plan and grant a deferral and grant a waiver

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.

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

gov.uk/mhra

Final Decision Letter

MHRA-101740-PIP01-24

Of 02/06/2025 17:59 BST

On the adopted decision for messenger RNA encoding Cas9; single guide RNA targeting the human KLKB1 gene (MHRA-101740-PIP01-24) 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 messenger RNA encoding Cas9; single guide RNA targeting the human KLKB1 gene, Dispersion for infusion , INTRAVENOUS USE .

This decision is addressed to Intellia Therapeutics, Inc., 40 Erie Street, Cambridge, UNITED STATES OF AMERICA, 02139

ANNEX I

1. Waiver

1.1 Condition:

Treatment of hereditary angioedema (HAE) The waiver applies / applied to: Paediatric Subset(s): The paediatric population from birth to less than 2 years of age Pharmaceutical form(s): Dispersion for infusion Route(s) of administration: INTRAVENOUS USE Reason for granting waiver: on the grounds that the specific medicinal product does not represent a significant therapeutic benefit as clinical studies(s) are not feasible

2. Paediatric Investigation Plan:

2.1 Condition(s):

Treatment of hereditary angioedema (HAE)

2.2 Indication(s) targeted by the PIP:

Treatment of hereditary angioedema (HAE)

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

The paediatric population from 2 years to less than 18 years of age

2.4 Pharmaceutical Form(s):

Dispersion 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	1	Study 1 (ITL-2002-CL-XXX) Open-label, single-arm trial to evaluate safety, pharmacokinetics, pharmacodynamics and activity in children from 2 years to less than 18 years of age with hereditary angioedema.
Extrapolation, Modeling & Simulation Studies	2	Study 2 Modelling and simulation analyses for the PK characterisation and dose finding in the target paediatric population to derive equivalent doses per age group for paediatric patients matching the same exposure values as those achieved in adult patients and to evaluate the use of the product in children from 2 years to less than 18 of age. Extrapolation plan Adult Phase 1/2 study (ITL-2002-CL-001), adult Phase 3 (ITL-2002-CL-301) study and PIP study (ITL-2002-CL-XXX) are part of the extrapolation plan of efficacy data from adult to the paediatric population from 2 years to less than 18 years of age with hereditary angioedema.
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:	Yes
Date of completion of the paediatric investigation plan:	31/08/2028
Deferral of one or more studies contained in the paediatric investigation plan:	Yes