EMA/28239/2024

European Medicines Agency decision

P/0071/2024

of 8 March 2024

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver for synthetic double-stranded siRNA oligonucleotide directed against apolipoprotein C-III mRNA and covalently linked to a ligand containing three N-acetylgalactosamine residues (ARO-APOC3) (EMEA-003420-PIP01-23) 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 Arrowhead Pharmaceuticals, Inc. on 24 April 2023 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 19 January 2024, in accordance with Article 17 of Regulation (EC) No 1901/2006 and Article 21 of said Regulation and Article 13 of said Regulation,

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 and on the granting of a deferral and on the granting of a waiver.

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

(3) It is therefore appropriate to adopt a decision granting a deferral.

(4) It is therefore appropriate to adopt a decision granting a waiver.

[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 synthetic double-stranded siRNA oligonucleotide directed against apolipoprotein C-III mRNA and covalently linked to a ligand containing three N-acetylgalactosamine residues (ARO-APOC3), solution for injection, subcutaneous 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

A deferral for synthetic double-stranded siRNA oligonucleotide directed against apolipoprotein C-III mRNA and covalently linked to a ligand containing three N-acetylgalactosamine residues (ARO-APOC3), solution for injection, subcutaneous 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 granted.

Article 3

A waiver for synthetic double-stranded siRNA oligonucleotide directed against apolipoprotein C-III mRNA and covalently linked to a ligand containing three N-acetylgalactosamine residues (ARO-APOC3), solution for injection, subcutaneous 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 granted.

Article 4

This decision is addressed to Arrowhead Pharmaceuticals, Inc., 177 East Colorado Boulevard, Suite 700, CA 91105 – Pasadena, USA.

EMA/PDCO/479730/2023 Corr[1]
Amsterdam, 19 January 2024

Opinion of the Paediatric Committee on the agreement of a Paediatric Investigation Plan and a deferral and a waiver

EMEA-003420-PIP01-23

Scope of the application

Active substance(s):

Synthetic double-stranded siRNA oligonucleotide directed against apolipoprotein C-III mRNA and covalently linked to a ligand containing three N-acetylgalactosamine residues (ARO-APOC3)

Invented name and authorisation status:

See Annex II

Condition(s):

Treatment of familial chylomicronaemia syndrome

Pharmaceutical form(s):

Solution for injection

Route(s) of administration:

Subcutaneous use

Name/corporate name of the PIP applicant:

Arrowhead Pharmaceuticals, Inc.

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, Arrowhead Pharmaceuticals, Inc. submitted for agreement to the European Medicines Agency on 24 April 2023 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 22 May 2023.

[1] 4 March 2024.

Supplementary information was provided by the applicant on 12 October 2023. The applicant proposed modifications to the paediatric investigation plan.

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;
   - to grant a deferral in accordance with Article 21 of said Regulation;
   - to grant a waiver for one or more subsets of the paediatric population in accordance with Article 13 of said Regulation and concluded in accordance with Article 11(1)(c) of said Regulation, on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments for paediatric patients.

   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 and the subset(s) of the paediatric population and condition(s) covered by the waiver 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 annexes 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

1.1. Condition:

Treatment of familial chylomicronaemia syndrome

The waiver applies to:

- the paediatric population from birth to less than 2 years of age;
- solution for injection, subcutaneous use;
- on the grounds that clinical studies with the specific medicinal product cannot be expected to be of significant therapeutic benefit to or fulfil a therapeutic need of the specified paediatric subset(s).

2. Paediatric investigation plan

2.1. Condition:

Treatment of familial chylomicronaemia syndrome

2.1.1. Indication(s) targeted by the PIP

Treatment of familial chylomicronaemia syndrome (FCS)

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

From 2 years of age to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Solution for injection

2.1.4. Measures

Area	Description
Quality-related studies	**Study 1** Development of a solution for injection for subcutaneous use in appropriate doses for children from 2 years of age to less than 12 years of age.
Non-clinical studies	Not applicable.
Clinical studies	**Study 2 (AROAPOC3-3007)** Open label study to evaluate the activity, pharmacokinetics, pharmacodynamics and safety of ARO-APOC3 in adolescents from 12 years to less than 18 years of age with familial chylomicronemia syndrome (FCS). **Study 3 (AROAPOC3-3007)** Open label study to evaluate the activity, pharmacokinetics, pharmacodynamics and safety of ARO-APOC3 in children from 2 years of age to less than 12 years of age with familial chylomicronaemia syndrome (FCS).

Modelling and simulation studies	**Study 4 (dose- finding, adolescents)** Modelling and simulation study to develop a population PK/PD model, using data from adults, to determine the appropriate dose in adolescents from 12 years of age to less than 18 years of age with FCS. **Study 5 (dose-finding, children from 2 years to less than 12 years of age)** Modelling and simulation study to develop a population PK/PD model, using data from adults, to determine the appropriate dose in children from 2 years of age to less than 12 years of age with FCS.
Other studies	Not applicable.
Extrapolation plan	Studies 2, 3, 4, and 5 are part of the extrapolation plan of PK and PD data from adult patients to the paediatric population from 2 years of age to less than 18 years of age with FCS.

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 February 2036
Deferral for one or more measures contained in the paediatric investigation plan:	Yes

Annex II

Information about the authorised medicinal product

Information provided by the applicant:

The product is not authorised anywhere in the European Community.