EMA/251491/2022

European Medicines Agency decision

P/0192/2022

of 10 June 2022

on the agreement of a paediatric investigation plan and on the granting of a waiver for sirolimus (EMEA-002982-PIP01-21) 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 Selecta Biosciences, Inc. on 22 February 2021 under Article 16(1) of Regulation (EC) No 1901/2006 also requesting a waiver under Article 13 of said Regulation,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 22 April 2022, in accordance with Article 17 of Regulation (EC) No 1901/2006 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 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 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 sirolimus, suspension 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

A waiver for sirolimus, suspension 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 granted.

Article 3

This decision is addressed to Selecta Biosciences, Inc., 65 Grove Street, MA 02472 – Watertown, USA.

EMA/PDCO/201426/2022
Amsterdam, 22 April 2022

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

EMEA-002982-PIP01-21

Scope of the application

Active substance(s):

Sirolimus

Condition(s):

Treatment of ornithine transcarbamylase deficiency

Pharmaceutical form(s):

Suspension for infusion

Route(s) of administration:

Intravenous use

Name/corporate name of the PIP applicant:

Selecta Biosciences, Inc.

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, Selecta Biosciences, Inc. submitted for agreement to the European Medicines Agency on 22 February 2021 an application for a paediatric investigation plan for the above mentioned medicinal product.

The procedure started on 27 April 2021.

Supplementary information was provided by the applicant on 23 January 2022. The applicant proposed modifications to the paediatric investigation plan and requested 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;
   - 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 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

1.1. Condition:

Treatment of ornithine transcarbamylase deficiency

The waiver applies to:

- the paediatric population from birth to less than 6 months of age;
- suspension for infusion, intravenous 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 ornithine transcarbamylase deficiency

2.1.1. Indication(s) targeted by the PIP

In combination with recombinant adeno-associated viral (rAAV) vector expressing the human ornithine transcarbamylase (hOTC) gene for the treatment of ornithine transcarbamylase deficiency in paediatric patients from 6 months to less than 18 years of age.

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

From 6 months to less than 18 years of age.

2.1.3. Pharmaceutical form(s)

Suspension for infusion

2.1.4. Measures

Area	**Description**
Quality-related studies	Not applicable.
Non-clinical studies	**Study 1** (same as study 1 in PIP EMEA-002983-PIP01-21) Juvenile animal study (PND 30) in an ornithine transcarbamylase spf-ash mouse model to evaluate the efficacy and safety of recombinant Adeno-associated virus serotype 8 vector expressing the human ornithine transcarbamylase gene (rAAV8-hOTC) (surrogate capsid) used alone or in combination with sirolimus (in biodegradable nanoparticle). **Study 2** (same as study 2 in PIP EMEA-002983-PIP01-21) Juvenile animal study (PND 14) in an ornithine transcarbamylase spf-ash mouse model to evaluate the efficacy and safety of recombinant

	Adeno-associated virus serotype 8 vector expressing the human ornithine transcarbamylase(gene (rAAV8-hOTC) (surrogate capsid) used alone or in combination with sirolimus (in biodegradable nanoparticle). **Study 3** In vivo study to evaluate the pharmacokinetics of sirolimus (in biodegradable nanoparticle) in an ornithine transcarbamylase spf-ash mouse model **Study 4** (same as study 4 in PIP EMEA-002983-PIP01-21) Single dose study to assess the toxicity, toxicokinetics and vector biodistribution of recombinant adeno-associated viral (rAAV) vector expressing the human ornithine transcarbamylase (hOTC) gene alone or in combination with sirolimus (in biodegradable nanoparticle) in adult non-human primates.
Clinical studies	**Study 5** (SEL-313/101, same as study 5 in PIP EMEA-002983-PIP01-21) Open label, dose escalation study to evaluate the safety and clinical activity of recombinant adeno-associated viral (rAAV) vector expressing the human ornithine transcarbamylase (hOTC) gene used in combination with sirolimus (in biodegradable nanoparticle) as add-on to standard of care in paediatric patients from 6 months to less than 18 years of age with ornithine transcarbamylase deficiency (OTCD). **Study 6** (SEL-313/301, same as study 6 in PIP EMEA-002983-PIP01-21) Randomised, open label, controlled study to evaluate the safety and efficacy of recombinant adeno-associated viral (rAAV) vector expressing the human ornithine transcarbamylase (hOTC) gene used in combination with sirolimus (in biodegradable nanoparticles) as add-on to standard of care compared to standard of care alone in paediatric patients from 6 months to less than 18 years of age with ornithine transcarbamylase deficiency (OTCD) with cross-over at week 28 to recombinant adeno-associated viral (rAAV) vector expressing the human ornithine transcarbamylase (hOTC) gene used in combination with sirolimus (in biodegradable nanoparticles) as add-on to standard of care in patients initially randomised to standard of care alone.
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:	Yes
Date of completion of the paediatric investigation plan:	By September 2029
Deferral for one or more measures contained in the paediatric investigation plan:	No