EMA/699630/2021

European Medicines Agency decision

P/0542/2021

of 31 December 2021

on the agreement of a paediatric investigation plan and on the granting of a deferral for repotrectinib (EMEA-002635-PIP02-21) 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 Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency[2],

Having regard to the application submitted by Premier Research SLU on 19 March 2021 under Article 16(1) of Regulation (EC) No 1901/2006 also requesting a deferral under Article 20 of said Regulation,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 12 November 2021, in accordance with Article 17 of Regulation (EC) No 1901/2006 and Article 21 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.

(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.

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

Has adopted this decision:

Article 1

A paediatric investigation plan for repotrectinib, capsule, hard, age-appropriate oral liquid dosage form, oral 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 repotrectinib, capsule, hard, age-appropriate oral liquid dosage form, oral 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 Premier Research SLU, 19 Camino de la Zarzuela, 1B 28023 – Madrid, Spain.

EMA/PDCO/455518/2021 Corr
Amsterdam, 12 November 2021

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

EMEA-002635-PIP02-21

Scope of the application

Active substance(s):

Repotrectinib

Condition(s):

Treatment of all conditions included in the category of malignant neoplasms (except haematopoietic neoplasms)

Pharmaceutical form(s):

Capsule, hard

Age-appropriate oral liquid dosage form

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Premier Research SLU

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, Premier Research SLU submitted for agreement to the European Medicines Agency on 19 March 2021 an application for a paediatric investigation plan for the above mentioned medicinal product and a deferral under Article 20 of said Regulation.

The procedure started on 27 April 2021.

Supplementary information was provided by the applicant on 6 August 2021. 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.

   The Norwegian Paediatric Committee member 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 all conditions included in the category of malignant neoplasms (except haematopoietic neoplasms)

2.1.1. Indication(s) targeted by the PIP

Treatment of patients with advanced or metastatic malignancies harbouring NTRK1-3 fusions that have been pretreated with a TRK tyrosine kinase inhibitor

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)

Capsule, hard; age-appropriate oral liquid dosage form

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	1	**Study 1** Development of an age-appropriate oral liquid dosage form
Non-clinical studies	2	**Study 2 (00480)** Dose range-finding juvenile toxicity study **Study 3 (00481)** Definitive juvenile toxicity study
Clinical studies	2	**Study 4 (TPX-0005-01/TRIDENT-1)** Open-label, two part, multiple dose, single arm trial to evaluate the recommended phase 2 dose (RP2D), pharmacokinetics and safety in adults (part 1) and safety and activity of the identified RP2D of repotrectinib in children from 12 years to less than 18 years of age (and adults) with advanced or metastatic cancer with NTRK1-3 genetic alterations and pretreated with a tyrosine kinase inhibitor (TKI).

		Study 5 (TPX-0005-07) Open-label, two part single arm trial to evaluate the recommended phase 2 dose (RP2D) (part 1), pharmacokinetics (PK), pharmacodynamics (PD), safety and activity of repotrectinib in children from birth to less than 18 years of age (and adults), enrolled in two cohorts with tyrosine kinase inhibitor (TKI) pre-treated solid tumours characterised by NTRK1-3 gene fusion (cohort 1) and solid tumours characterised by other ALK/ROS1/NTRK1-3 alterations or NTRK fusions without centrally confirmed measurable disease not otherwise eligible for cohort 1.
Extrapolation, modelling and simulation studies	2	**Study 6** Modelling and simulation study to support the dose finding of the product in children from birth to less than 18 years of age with advanced or metastatic malignancies harbouring NTRK1-3 fusions that have been pretreated with a TRK tyrosine kinase inhibitor. **Study 7** Modelling and simulation study to evaluate the use of the product in children from birth to less than 18 years of age with advanced or metastatic malignancies harbouring NTRK1-3 fusions that have been pretreated with a TRK tyrosine kinase inhibitor.
Other studies	0	Not applicable
Other measures	0	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 December 2023
Deferral for one or more measures contained in the paediatric investigation plan:	Yes