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

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Decision Cover Letter

Decision of the licensing authority to:

agree a paediatric investigation plan and grant a deferral

MHRA-100787-PIP01-22

Scope of the Application

Active Substance(s)

Repotrectinib

Condition(s)

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

Pharmaceutical Form(s)

Capsule, hard; Oral suspension

Route(s) of Administration

ORAL USE

Name / Corporate name of the PIP applicant

BRISTOL-MYERS SQUIBB PHARMA EEIG

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, BRISTOL-MYERS SQUIBB PHARMA EEIG submitted to the licensing authority on 25/01/2023 13:10 GMT an application for a Paediatric Investigation Plan

The procedure started on 15/06/2023 11:52 BST

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

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.

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Final Decision Letter

MHRA-100787-PIP01-22

Of 21/08/2023 16:20 BST

On the adopted decision for Repotrectinib (MHRA-100787-PIP01-22) 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 Repotrectinib, Capsule, hard; Oral suspension , ORAL USE .

This decision is addressed to BRISTOL-MYERS SQUIBB PHARMA EEIG, Plaza 254, Blanchardstown Corporate Park 2, Dublin, IRELAND, D15 T867

ANNEX I

1. Waiver

1.1 Condition:

Not applicable

2. Paediatric Investigation Plan:

2.1 Condition(s):

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

2.2 Indication(s) targeted by the PIP:

Treatment of patients with advanced or metastatic malignancies harbouring NTRK1-3 fusions that have been pre-treated with a TRK tyrosine kinase inhibitor (TKI)

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

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

2.4 Pharmaceutical Form(s):

Capsule, hard Oral suspension

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	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	1	Study 4 (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, Modeling & Simulation Studies	2	Study 5 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 pre-treated with a TRK tyrosine kinase inhibitor. Study 6 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 pre-treated with a TRK tyrosine kinase inhibitor.
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:	30/11/2025
Deferral of one or more studies contained in the paediatric investigation plan:	Yes