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

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Decision Cover Letter

Decision of the licensing authority to:

accept change(s) to the agreed paediatric investigation plan and to the deferral

MHRA-101249-PIP01-23-M01

Scope of the Application

Active Substance(s)

Tovorafenib

Condition(s)

Treatment of paediatric low grade glioma

Pharmaceutical Form(s)

Tablet, Age-appropriate oral liquid dosage form

Route(s) of Administration

ORAL USE

Name / Corporate name of the PIP applicant

Day One Biopharmaceuticals, Inc

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, Day One Biopharmaceuticals, Inc submitted to the licensing authority on 12/12/2023 10:16 GMT an application for a Modification

The procedure started on 15/02/2024 13:41 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 accept change(s) to the agreed paediatric investigation plan and to the 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-101249-PIP01-23-M01

Of 27/02/2024 15:45 GMT

On the adopted decision for Tovorafenib (MHRA-101249-PIP01-23-M01) 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 modification of a paediatric investigation plan (including modification of a waiver or deferral included in that paediatric investigation plan).

This decision applies to a Modification for Tovorafenib, Tablet Age-appropriate oral liquid dosage form , ORAL USE .

This decision is addressed to Day One Biopharmaceuticals, Inc, 2000 Sierra Point Parkway Suite 501, Brisbane, UNITED STATES OF AMERICA, 94005-1874

ANNEX I

1. Waiver

1.1 Condition:

Treatment of paediatric low grade glioma. The waiver applies / applied to: Paediatric Subset(s): The paediatric population from birth to less than 6 months of age. Pharmaceutical form(s): Tablet. Age-appropriate oral liquid dosage form. Route(s) of administration: ORAL 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 paediatric low grade glioma.

2.2 Indication(s) targeted by the PIP:

Treatment of patients newly diagnosed with unresectable or sub-totally resected low-grade glioma harbouring BRAF fusion. Treatment of relapsed or refractory patients with low grade glioma harbouring BRAF fusion.

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

The paediatric population from 6 months to less than 18 years of age.

2.4 Pharmaceutical Form(s):

Tablet. Age-appropriate oral liquid dosage form.

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	1	Study 1 Development of an age-appropriate formulation.
Non-Clinical Studies	0	Not applicable.
Clinical Studies	2	Study 2 Deleted during procedure MHRA-101249-PIP01-23-M01. Study 3 (FIREFLY-1) Open-label, single arm trial, to evaluate pharmacokinetics, safety and activity of DAY101 in children from 6 months to less than 18 years of age (and adults up 25 years) with RAF-altered, recurrent or progressive low grade glioma. Study 4 (FIREFLY-2 / LOGGIC) Randomised controlled, open label trial to evaluate safety and efficacy of DAY101 in children from 6 months to less than 18 years of age (and adults up to 25 years) with newly diagnosed unresectable or sub-totally resected low-grade glioma harbouring an activating RAF alteration.
Extrapolation, Modeling & Simulation Studies	1	Study 5 Modelling and simulation study to confirm or modify the paediatric posology in children from 6 months to less than 18 years of age with low grade glioma.
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:	31/07/2030
Deferral of one or more studies contained in the paediatric investigation plan:	Yes