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 waiver

MHRA-101573-PIP01-24

Scope of the Application

Active Substance(s)

Trofinetide

Condition(s)

Treatment of Rett syndrome

Pharmaceutical Form(s)

Oral solution

Route(s) of Administration

ORAL USE, GASTROENTERAL USE

Name / Corporate name of the PIP applicant

Acadia Pharmaceuticals Inc.

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, Acadia Pharmaceuticals Inc. submitted to the licensing authority on 09/09/2024 10:28 BST an application for a Paediatric Investigation Plan

The procedure started on 25/10/2024 11:34 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 waiver

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-101573-PIP01-24

Of 05/12/2024 09:33 GMT

On the adopted decision for Trofinetide (MHRA-101573-PIP01-24) 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 Trofinetide, Oral solution , ORAL USE, GASTROENTERAL USE .

This decision is addressed to Acadia Pharmaceuticals Inc., 12830 El Camino Real, Suite 400, San Diego, UNITED STATES OF AMERICA, 92130

ANNEX I

1. Waiver

1.1 Condition:

Treatment of Rett syndrome The waiver applies / applied to: Paediatric Subset(s): The paediatric population from birth to less than 2 years of age Pharmaceutical form(s): Oral solution Route(s) of administration: ORAL USE GASTROENTERAL USE Reason for granting waiver: on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments

2. Paediatric Investigation Plan:

2.1 Condition(s):

Treatment of Rett syndrome

2.2 Indication(s) targeted by the PIP:

Treatment of Rett syndrome (RTT)

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

The paediatric population from 2 years to less than 18 years of age

2.4 Pharmaceutical Form(s):

Oral solution

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	0	Not applicable.
Non-Clinical Studies	2	Study 1 (0621-16031) Repeat-dose oral dosage study in juvenile rats to evaluate the toxicity, and toxicokinetic profile and reversibility of possible toxicity or effects on development of trofinetide. Study 2 (0621-16032) Repeat-dose oral dosage study in juvenile dogs to evaluate the toxicity, and toxicokinetic profile and reversibility of possible toxicity or effects on development of trofinetide.
Clinical Studies	6	Study 3 (Neu-2566-RETT-001) Randomised, double-blind, placebo-controlled, dose- escalation study of trofinetide in female paediatric patients from 16 years to less than 18 years of age (and adult females) with RTT. Study 4 (Neu-2566-RETT-002) Randomised, double-blind, placebo-controlled, parallel group, dose-ranging study of the safety, pharmacokinetics and efficacy of trofinetide in female paediatric patients aged from 5 years to less than 16 years of age diagnosed with post-regression, classic Rett syndrome. Study 5 (ACP-2566-003) Randomised, double-blind, placebo-controlled, parallel group study to evaluate efficacy, safety and pharmacokinetics

		of trofinetide in female subjects from 5 years to less than 18 years of age diagnosed with post- regression, classic Rett syndrome. Study 6 (ACP-2566-004) 40-week open-label extension study to evaluate the long- term safety, tolerability, efficacy, and pharmacokinetics of trofinetide in paediatric and adult patients with RTT who completed PIP Study 5 (ACP-2566-003). Study 7 (ACP-2566-005) 32-month, multicentre, open-label extension study to evaluate long-term safety and tolerability of trofinetide in paediatric and adult patients with RTT who completed PIP Study 6 study (Study ACP-2566-004). Study 8 (ACP-2566-009) Open-label study to evaluate safety and tolerability, pharmacokinetics, and efficacy of trofinetide in female paediatric subjects from 2 years to less than 5 years of age with Rett syndrome.
Extrapolation, Modeling & Simulation Studies	2	Study 9 (ACP-2566-MS-007, ACP-2566-MS-008, ACP-2566-MS-010, ACP-2566-MS-009) Population pharmacokinetic model to establish the dose of trofinetide to be used in paediatric patients and exposure-response (E-R) model to confirm appropriateness of target exposure and support extrapolation of efficacy in patients below 5 years of age. Extrapolation plan Studies 5, 8 and 9, are part of the extrapolation plan of efficacy data from paediatric patients above 5 years of age to the paediatric population from 2 years to less than 5 years of age.
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:	No
Date of completion of the paediatric investigation plan:	30/06/2023
Deferral of one or more studies contained in the paediatric investigation plan:	No