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-101120-PIP01-23

Scope of the Application

Active Substance(s)

RVT-802 (allogeneic cultured postnatal thymus tissue-derived product)

Condition(s)

Treatment of congenital athymia

Pharmaceutical Form(s)

Living tissue equivalent

Route(s) of Administration

IMPLANTATION USE

Name / Corporate name of the PIP applicant

Myovant Sciences Ireland Limited

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, Myovant Sciences Ireland Limited submitted to the licensing authority on 07/08/2023 13:57 BST an application for a Paediatric Investigation Plan

The procedure started on 18/10/2023 08:48 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-101120-PIP01-23

Of 15/07/2024 08:41 BST

On the adopted decision for RVT-802 (allogeneic cultured postnatal thymus tissue-derived product) (MHRA-101120-PIP01-23) 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 RVT-802 (allogeneic cultured postnatal thymus tissue-derived product), Living tissue equivalent , IMPLANTATION USE .

This decision is addressed to Myovant Sciences Ireland Limited, Rocktwist House Block 1, Western Business Park, Shannon, IRELAND, V14 FW97

ANNEX I

1. Waiver

1.1 Condition:

Not applicable.

2. Paediatric Investigation Plan:

2.1 Condition(s):

Treatment of congenital athymia

2.2 Indication(s) targeted by the PIP:

Immune reconstitution in paediatric patients with congenital athymia

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

All subsets of the paediatric population from birth to less than 18 years of age

2.4 Pharmaceutical Form(s):

Living tissue equivalent

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	0	Not applicable.
Non-Clinical Studies	2	Study 1 (RVT-802-001 [HRT 11]) Study to evaluate the feasibility and efficacy of allogenic neonatal thymus transplantation (fresh, after cryopreservation of the fresh thymus, or after 8 days of culture of the neonatal thymus) in nude rats leading to thymopoiesis with resulting T cell development. Study 2 (RVT-802-001 [HRT 13]) Allogeneic thymus transplantation study in nude rats to evaluate the feasibility and efficacy of neonatal thymus transplantation leading to thymopoiesis with resulting T cell development 9 months post-transplant.
Clinical Studies	5	Study 3 (668-1) Open label, non-randomised trial to evaluate safety, activity and immune reconstitution following transplantation of allogeneic cultured postnatal thymus in children from birth to less than 18 years of age with congenital athymia secondary to congenital DiGeorge Anomaly (cDGA). Study 4 (668-2) Open label, non-randomised trial to evaluate safety, efficacy, and immune reconstitution following transplantation of allogeneic cultured postnatal thymus (RVT-802) in children from birth to less than 18 years of age with congenital athymia. Study 5 (884) Open label non-randomised single centre trial

		to evaluate safety, tolerability, and efficacy of allogeneic cultured postnatal thymus (RVT-802) in children with congenital athymia receiving immunosuppression. Study 6 (931) Open label, non-randomised study to evaluate safety, tolerability and efficacy of allogeneic cultured postnatal thymus (RVT-802) and parental parathyroid transplantation in children from birth to less than 18 years of age with typical and atypical congenital Di-George Anomaly (cDGA) and with hypoparathyroidism requiring calcium supplementation. Study 7 (932) Open label, non-randomised study to evaluate safety and to establish the dose of allogeneic cultured postnatal thymus (RVT-802) and correlate immunological outcomes post-transplant in children from birth to less than 18 years of age with typical cDGA not receiving immunosuppression.
Extrapolation, Modeling & Simulation Studies	0	Not applicable.
Other Studies	5	Study 8 (950) Open label, non-randomised single centre study to evaluate safety, tolerability, and efficacy of allogeneic cultured postnatal thymus (RVT-802) transplant in children with congenital athymia (typical or atypical cDGA) and receiving immune suppression based on individual phytohaemagglutinin (PHA) responses. Study 9 (25966) Open label, non-randomised single centre study to evaluate safety, tolerability, and efficacy of RVT-802 in children with congenital athymia (typical or atypical cDGA) receiving immune suppression tailored to individual immune status. Study 10 (51692) Open label, non-randomised, expanded access study to evaluate safety, tolerability and efficacy of RVT-802 in children from birth to less than 18 years of age with immunodeficiency, hematologic malignancies, or severe autoimmune disease associated with

		poor thymic function. Study 11 (RVT-802-4001) Open label, single arm non-randomised, observational study to evaluate long term efficacy and safety of RVT-802 in children from birth to less than 18 years of age diagnosed with congenital athymia who are scheduled to have or have recently been implanted with RVT-802. Study 12 Pooled analysis of safety and efficacy of cultured, allogenic thymic tissue (RVT-802) for transplantation in children from birth to less than 18 years of age with primary immune deficiency resulting from congenital athymia associated with complete DiGeorge Anomaly (cDGA) or forkhead box protein N1 (FOXN1) deficiency.
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:	30/04/2026
Deferral of one or more studies contained in the paediatric investigation plan:	Yes