To:

Head of Paediatric Medicines
European Medicines Agency

Notification of discontinuation of a paediatric development which is covered by an agreed PIP Decision

Actives substances(s): lademirsen

Invented name: NA

Latest Decision number(s): 1) P/0336/2022

Corresponding PIP number(s): 1) EMEA-003064-PIP01-21

Date of initial marketing authorisation granted: NA

Date of authorisation of new indication, pharmaceutical form or route of administration: NA

Please note that development of the medicinal product above in the following **condition(s)/indication(s)**:

Treatment of Alport syndrome

☒ has been discontinued

☐ has been suspended/put on long-term hold (with possible re-start at a later time)

for the following reason(s): (tick all that apply)

☒ (possible) lack of efficacy in adults

☐ (possible) lack of efficacy in children

☐ (possible) unsatisfactory safety profile in adults

☐ (possible) unsatisfactory safety profile in children

☐ commercial reasons (please specify:)

☐ manufacturing / quality problems

☐ other regulatory action (please specify:) (e.g. suspension, revocation of M.A.)

☐ other reason (please specify:)

Please add a brief description (max 2000 characters) of the reason(s) for the discontinuation / suspension:

On 01 June 2022, The Data Monitoring Committee (DMC) reviewed and evaluated the output of the futility analysis from study ACT16248.

The futility analysis was conducted after 24 participants from Stage-1 completed 24 weeks of treatment. At that time 55% of participants had completed 24 weeks of treatment.

Unfortunately, based on the prespecified futility criteria the analysis did not demonstrate that lademirsen provided a meaningful difference in the primary endpoint (annualized change in estimated glomerular filtration rate (eGFR) from baseline to 48 weeks). Therefore, the sponsor has decided to follow the recommendation from the DMC, to terminate study ACT16248 and the Alport clinical development program. The decision to terminate the study is not driven by safety concerns and the safety profile of lademirsen remains as reported earlier.

Please note that if the PIP has been submitted as part of a marketing authorisation application in order to comply with the requirements of Article 7 of the Paediatric Regulation (as a condition of the validation of the respective application) and a marketing authorisation was granted based on this application, then there is a legal obligation to complete that PIP. The same applies if there has been a successful post-authorisation application, where the PIP was included in order to comply with the requirements of Article 8 of the Paediatric Regulation.

Please confirm if any of the above applies to the PIP in question:

Yes ☐ No ☒

If yes, it means that based on the Marketing Authorisation obtained at the end of that initial procedure or the successful post-authorisation application, as applicable, you are obliged to complete that PIP. That obligation cannot be cancelled by a unilateral decision, including by withdrawing the MA. Such PIP must be completed, unless it is modified in agreement with the PDCO by removing all outstanding PIP measures or granting a full product-specific waiver instead (upon relevant circumstances in accordance with the Paediatric Regulation). Non-completion of a binding PIP establishes noncompliance with the requirements of the Paediatric Regulation, which the European Medicines Agency has an obligation to report to the European Commission.

Name and signature of the PIP contact point:	signature on file
Date:	02/05/2023
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