

DG PRE/Afdeling R&D/CTR

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GMO Dossier B/BE/26/BVW2 (2025-522207-15-01): An Open-label, Multicenter, Two Part, Ascending Dose Followed by a Controlled Trial to Assess the Safety and Efficacy of a Subretinal Administration of AAVB-039 in Participants with Stargardt Disease (STGD1) (CELESTE)

Wij informeren u dat uw vergunningsaanvraag werd goedgekeurd.

De vergunning is conform het koninklijk besluit van 21 februari 2005 tot reglementering van de doelbewuste introductie in het leefmilieu evenals van het in de handel brengen van genetisch gemodificeerde organismen of van producten die er bevatten.

(http://www.ejustice.just.fgov.be/cgi_loi/change_lg.pl?language=nl&la=N&cn=2005022131&table_name=wet)

Uw vergunning wordt verleend op basis van het gunstig advies van de Adviesraad voor Bioveiligheid van 4 juni 2026, onder de voorwaarden die in de conclusie van bovengenoemd advies zijn vermeld, namelijk:

Based on the scientific assessment of the notification made by the Belgian experts, the Biosafety Advisory Council concludes that it is unlikely that AAVB-039 developed to treat patients with Stargardt Disease, by means of endogenous production of a functional human ABCA4 protein transporter to the retina of patients, will have any adverse effects on human health or on the environment in the context of the intended clinical trial provided that all the foreseen safety measures are followed.

Therefore, the Biosafety Advisory Council issues a **positive advice with the following conditions:**

- The notifier and the investigators must strictly apply the clinical trial protocol, and all the safety instructions as described in the following documents :

- o Latest version of the ICF
- o Latest version of the Protocol
- o SNIF public and confidential v3.0
- o CAF_v3.0_non confidential
- o CAF_confidential
- o M24-528 – Investigative Site Pharmacy Manual_v3.0

- As committed by the applicant in his responses to SBB requests on 20-Apr-2026, the ICF will be updated by adding the recommendation to refrain from donation of blood, organs, tissues, and cells.

- As committed by the applicant, the ICF will be updated to include clear instructions regarding eye dressing management. Specifically, the treated eye will be covered with an ocular patch and protective eye shield for a minimum of 7 days, in accordance with local clinical practice. Participants and their family members/caregivers will be instructed not to touch or rub the treated eye, to maintain appropriate hand hygiene, and to wear gloves when contact with bodily fluids is anticipated. In addition, all used dressings,

tissues, swabs, and other potentially contaminated materials should be placed in sealed bags prior to disposal. Updated ICF will be submitted for Belgium Ethics Committee in the next substantial modification.

- In both SNIF documents (public and confidential) will be updated as follows and provided as soon as possible: the use of alcohol wipes following disinfection with 10% bleach (0,5% sodium hypochlorite) is still described. However, as previously indicated, bleach solutions should not be used in combination with alcohol wipes, as this may produce toxic chloroform vapours. Therefore, both documents should be revised either by removing the recommendation to use alcohol wipes or by specifying that the sodium hypochlorite solution must first be neutralized using a 3% sodium thiosulfate solution prior any application of alcohol. Since alcohol is not considered as an effective disinfectant against AAV, we recommend avoiding the use of alcohol-based wipes altogether.

- Any protocol amendment has to be previously approved by the Competent Authority.

- The notifier is responsible to verify that each study centre has qualified personnel experienced in handling infectious material and that the investigator has the required authorizations to perform the clinical trial activities inside the hospital (laboratory, pharmacy, hospital room, consultation room...) according to the Regional Decrees transposing Directive 2009/41/EC on Contained use of genetically modified micro-organisms.

- The Biosafety Advisory Council should be informed within two weeks when the first patient starts the treatment and the last patient receives the last treatment.

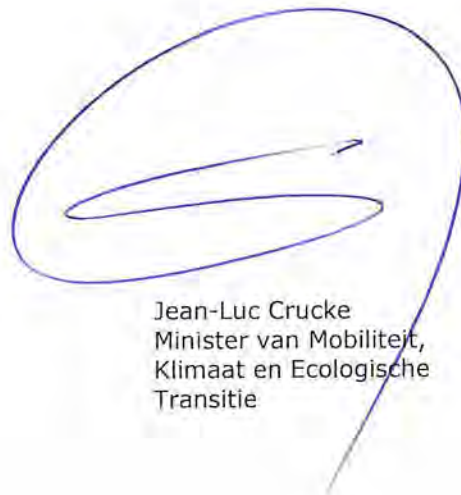
- At the latest six months after the last visit of the last patient included in the trial, the notifier must send to the competent authority at the attention of the Biosafety Advisory Council a report with details concerning the biosafety aspects of the project. This report will contain as a minimum:

- o The total number of patients enrolled in the trial and the number of patients from Belgium;
- o A summary of all adverse events documented by the investigators as likely or definitely related to the study medication;
- o A report on the accidental releases, if any, of AAVB-039.

Hoogachtend,



Frank Vandenbroucke
Vice-eersteminister en
minister van Sociale Zaken en
Volksgezondheid, belast met
Armoedebestrijding



Jean-Luc Crucke
Minister van Mobiliteit,
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