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uw bericht van	uw kenmerk	ons kenmerk	bijlagen	datum
		FAGG/DGPRE/R&D/[redacted]		07.11.2025

Dossier GMO: B-BE-25-BVW5 (2024-510581-17-00): *(ASK-CHF2-CS201) A Phase 2, adaptive, double-blinded, placebo-controlled, randomized, multi-center trial to evaluate the efficacy, safety and tolerability of intracoronary infusion of AB-1002 in adult subjects with New York Heart Association (NYHA) Class III heart failure and non-ischemic cardiomyopathy*

Geachte [redacted]

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 13 oktober 2025, 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 expert, the Biosafety Advisory Council concludes that it is unlikely that AB-1002 developed to treat patients with NYHA Class III heart failure and non-ischemic cardiomyopathy, by means of endogenous production of Inhibitor-1c 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 :*
  - *Latest version of the ICF*
  - *Latest version of the Protocol*
  - *SNIF*
  - *AB-1002_CAF_AAV_Non Confidential_BE_25Aug25*
  - *AB-1002_CAF_AAV_Confidential*
  - *AB-1002_Safety Instructions for staff_v2_25Aug25*
  - *ASK-CHF2-CS201_GenePHIT_Patient Information Sheet_Viral Shedding Best Practices_v1.0_22Aug25*

- *As committed by the applicant, some documents still need to be updated as follows in the next amendment opportunity:*
  - *The protocol and all related documents will be updated in order to extent the contraception duration and restrictions on sperm donation to a period of up to 1 year post-treatment*

- *IB (Investigator Brochure) : the dosing information, specifically whether the dose of 1E13 vg or 1E14 vg is per kg or per animal, will be clearly indicate throughout the entire document*
- *IB : Biodistribution results from animals studies reported in section 4.4.1.3 of the IB appear to contradict data presented in section 4.3.2, which refers to systemic biodistribution studies of pre-clinical models from Asokan et al. (2010) suggesting that AAV2i8 is not expected to be distributed throughout the body in significant amounts. The applicant will update the relevant sections to ensure consistency and accuracy across the documentation*
- *IB : As vector biodistribution is highly species-specific and differences in serotype and vector design strictly limit the extrapolation of preclinical data to humans, the applicant will avoid speculating in section 4.4.5 (p33/58) about the absence of persistence of vector DNA signal in the patients*
- *IB : in section 6.6, "pregndoant" will be corrected into "pregnant"*
- *Protocol : in section 2.3.1 (p25/97), the following sentence "It is possible that AB-1002 could interact with other viruses with which the subject comes in contact, forming a new virus that could produce new side effects. However, this is unlikely to occur." Will be corrected in a more appropriate phrasing such as : "The potential formation of a new virus via the interaction between AB-1002 and another exogenous or endogenous virus coming into contact with the patient, has the potential to provoke new side effects; however, this is highly unlikely to occur."*
- *ICF_NL : on page 11/38, "een virus wordt gebruikt als vector" will be corrected into "een virale vector wordt gebruikt om genetische info over te brengen" and "genvirusproduct" will be changed to "AAV vector" or "viral vector"*
- *ICF_FR : on page 12/39, "une thérapie génique utilisant un virus comme vecteur" will be corrected into "un vecteur viral est utilisé pour transférer des informations génétiques" and on page 15/39, "Le produit viral du gène" will be changed to "Le vecteur AAV" ou « Le vecteur viral ».*

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

- *The notifier is responsible to verify that each study center 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 at least contain:*
  - *The total number of patients included in the trial and the number of patients included in Belgium;*
  - *A summary of all adverse events marked by the investigators as probably or definitely related to the study medication;*
  - *A report on the accidental releases, if any, of AB-1002."*

Hoogachtend,

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

Jean-Luc Crucke
Minister van Mobiliteit,
Klimaat en Ecologische
Transitie