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uw bericht van	uw kenmerk	ons kenmerk	bijlagen	datum
		FAGG/DGPRE/R&[redacted]		28.06.2024

Dossier GMO: B/BE/24/BVW5 (2022-502844-11-00): C0371002 - Phase 3, open-label, single-arm study to evaluate efficacy and safety of FIX gene transfer with PF-06838435 (rAAV-Spark100-hFIX-R338L) in adult male participants with moderately severe to severe hemophilia B (FIX:C≤2%) (BeneGene-2)

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 31 mei 2024, 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 PF-06838435 developed as a gene therapy approach for the treatment of Hemophilia B will have adverse effects on human health or on the environment in the context of the intended clinical trial provided that all of the foreseen safety measures are followed as described in the following updated documents:

- *IP Manual for staff_v7 (14May2024)*
- *SDS Fidavec (28 June 2023)*
- *Main ICD V1_28Nov2023*
- *CAF Public_BE (16 May 2024)*
- *CAF Confidential Annex_BE (04 April 2024)*
- *SNIF_Belgium (16 May 2024)*
- *Patient Special Instructions Summary (17 May 2024)*
- *Technical Sheet for Investigation Product (IP) Handling_v2.0 (06 May 2024)*
- *Addendum 2 GMO_V1.0 (16 May 2024)*

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

- The notifier and the investigators must strictly apply the approved clinical trial protocol, and all the safety instructions as described in the dossier and the updated/new documents listed here above.

- The notifier makes sure patients are well informed about the instructions to be applied regarding blood, organs, tissues and cells for transplantation or donation. Furthermore, as confirmed by the applicant, recommendations for donating blood, organs, tissues and cells for transplantation and

the length of time they must applied, will be included in the next version of the Informed Consent Document at the next substantial amendment.

- The study specific instructions for caregivers that will visit patients at home must be updated by detailing the PPE to be used during the visit and by specifying the minimum contact time of the decontamination solution with the spill in case of accidental spill (section III).

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

- The notifier is responsible to verify that the 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.

- At the latest 15 days after the start of the trial, the notifier should provide, along with the delivery of the control sample, a detailed protocol for the method of conservation and analysis of the control sample.

- 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 shall at least contain:

- *o The total number of patients included in the trial and the number of patients included in Belgium;*
- *o A summary of all adverse events marked by the investigators as probably or definitely related to the study medication;*
- *o A report on the accidental releases, if any, of PF-06838435."*

Hoogachtend,

Frank Vandenbroucke
Vice-eersteminister en
minister van Volksgezondheid
en Sociale Zaken

Zakia Khattabi
Minister van Klimaat,
Leefmilieu, Duurzame
Ontwikkeling en Green Deal