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

Dossier GMO: B/BE/21/BVW8 (2020-002873-88 en 2020-002255-37):
-2020-002873-88 - Phase 3 Randomized, Controlled Study of AAV5-hRKp.RPGR for the Treatment of X-linked Retinitis Pigmentosa Associated with Variants in the RPGR gene
-2020-002255-37 - Phase 3 Follow-up Study of AAV5-hRKp.RPGR for the Treatment of X-linked Retinitis Pigmentosa Associated with Variants in the RPGR gene

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 19 april 2022, 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 AAV5-hRKp.RPGR developed as a gene therapy approach for the treatment of X-linked Retinitis Pigmentosa Associated with Variants in the RPGRgene, will have 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 as described in the following updated documents (and for some still to be adapted in accordance with the conditions stipulated below):*

- *3.1.MGT-RPGR-021_GMO_AAV_CAF_clean_17Mar22*
- *4.1.021_022_GMO_AAV_CAF confidential annex_clean_17Mar22*
- *6.0 Safety statement AAV v1.4 BE-15Mar22 (Biosafety Instructions for handling AAV5-hRKp.RPGR for health care workers and staff) – to be updated in accordance with condition 2*
- *2020-002873-88_MGT-RPGR-021_Protocol_amend 5_15JUL2021- to be updated in accordance with condition 4 here below*
- *MGT-RPGR-021_22 ICF Addendum Take home summary_V1.0_18Mar2022-version ENG_DUT_ and FRE - to be updated in accordance with condition 5 here below*

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

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

2. With respect to the Biosafety Instructions for handling AAV5-hRKp.RPGR for health care workers and staff, it should be indicated that the preparation of the IMP for administration is recommended to be conducted in a biological safety cabinet. The use of goggles and mask are mandatory should the use of a biosafety cabinet not be possible (e.g. handling of spill incident and administration of the IMP to the patient).

3. The notifier takes due account of its commitment to report shedding data obtained from the ongoing (study MGT009) and planned clinical trials in view of any further step in the clinical development of AAV5-hRKp.RPGR.

4. The notifier should continue the collection of shedding data until two consecutive results are at or below the limit of detection as determined for each of the matrices. The notifier is required to update the protocol for study MGT-RPGR-021 accordingly. In addition, the notifier is requested to consider the collection of shedding data on lacrimal fluid (tear) from both eyes, saliva, whole blood and serum samples for study MGT-RPGR-022 as well.

5. The notifier should indicate in document MGT-RPGR-021_22 ICF Addendum Take home summary_V1.0_18Mar2022_version ENG_DUT_and FRE that the saliva from patients treated with AAV5-hRKp.RPGR may also contain viral vector genome.

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

7. 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 authorisations 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 the contained use of genetically modified micro-organisms.

8. The BAC should be informed within two weeks when the first patient starts the treatment and the last patient receives the last treatment.

9. At the latest six months after the last visit of the last patient included in the trial, the notifier must send the competent authority for the attention of the BAC a report with details concerning the biosafety aspects of the project. This report shall contain at least:
a. The total number of patients included in the trial and the number of patients included in Belgium;
b. A summary of all adverse events marked by the investigators as probably or definitely related to the study medication;
c. A report on the accidental releases, if any, of AAV5-hRKp.RPGR."

Hoogachtend,

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

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