Federaal Agentschap voor Geneesmiddelen en Gezondheidsproducten
Galileelaan 5/03
1210 BRUSSEL

www.fagg.be

DG PRE vergunning/afdeling Onderzoek en Ontwikkeling

[redacted]
Tel.: +32 2 528 [redacted]
Fax: +32 2 528 [redacted]
[redacted]

IQVIA Biotech
[redacted]
Business & Technology Centre
Bessemer Drive, Stevenage
Hertfordshire, SG1 2DX
United Kingdom

| uw bericht van | uw kenmerk | ons kenmerk | bijlagen | datum |
|---|---|---|---|---|
| | | FAGG/DGPRE/R&D/VDC | | 14.03.2022 |

**Dossier GMO: B/BE/21/BVW4 (2019-000728-16): An Open-Label, Multicenter, Non-Randomized, Dose-Confirmation and Cohort-Expansion Phase 1b Study to Evaluate the Safety, Tolerability, and Anti-Tumor Activity of ATP128, VSV-GP128 and BI 754091, in Patients with Stage IV Colorectal Cancer**

Geachte mevrouw [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 17 februari 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 expert, the Biosafety Advisory Council concludes that it is unlikely that VSV-GP128 developed as a gene therapy approach for the treatment of Stage IV Colorectal Cancer 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 new or updated documents:*

- *1.3a KISIMA-01_CAF_VSV_GP128_Clean_24Jan2022*
- *1.4 KISIMA-01_VSV-GP128 Instructions for study site personal*
- *1.5 KISIMA-01_Intructions for participants*

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

*- Referring to the vector-borne properties of the wt-VSV, and as a precautionary measure, the patient should be recommended to use mosquito repellent during the day and the night (alternatively a mosquito net could be used when sleeping) for 7 days, unless the notifier can provide supporting evidence on the low likelihood of transmission through arthropod vectors. In this regard, the notifier is asked to clarify whether any replication data of VSV-GP128 in arthropods are available (e.g. replication data in relevant arthropod cell cultures or live mosquitoes).*

*- The notifier and the investigators must strictly apply the clinical trial protocol version 10, and all the safety instructions as described in the dossier and the updated and new documents listed here above.*

*- Any protocol amendment has to 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 report of the shedding data obtained from the clinical trial (monitoring of viral vector excretion/secretion in buccal swabs, nasal swabs and urine samples after injection at Day 15 (pre-dosing), Day 15 (1h post-dosing), Day 15 (8h post-dosing), Days 19-22-29-36 compared to baseline);*
*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 VSV-GP128."*

Hoogachtend,

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

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