Framework of research and development for a proposed Deliberate Release of a

Genetically Modified Organism

MeiraGTx UK II Limited, 92 Britannia Walk, London, N1 7NQ, United Kingdom in accordance the Deliberate Release Directive 2001/18/EC has given notification to the Federal Agency for Medicines and Health Products (FAMHP) in Belgium, of a proposal to release the Genetically Modified Organism (GMO), AAV5-hRKp.RPGR, for the conduct of clinical trials:

- MGT-RPGR-021: Phase 3 Randomized, Controlled Study of AAV5-hRKp.RPGR for the Treatment of X-linked Retinitis Pigmentosa Associated with Variants in the RPGR gene; and
- MGT-RPGR-022: Phase 3 Follow-up Study of AAV5-hRKp.RPGR for the Treatment of X-linked Retinitis Pigmentosa Associated with Variants in the RPGR gene.

Description of the genetically modified organism

AAV5-hRKp.RPGR is a gene therapy product derived from a recombinant, replication-incompetent, adeno-associated virus (AAV) viral vector with a serotype 5 capsid (AAV5).

AAV5-hRKp.RPGR is currently being developed for patients with X-linked retinitis pigmentosa (XLRP) caused by mutations in the human retinitis pigmentosa guanosine triphosphatase regulator (RPGR) gene.

The Purpose of the proposed Deliberate Release

The purpose of clinical trial MGT-RPGR-021 is to study AAV5-hRKp.RPGR for the treatment of XLRP and the purpose of clinical trial MGT-RPGR-022 is to follow-up on participants treated with AAV5-hRKp.RPGR during the MGT-RPGR-021 clinical trial and allow for the initial treatment of participants who were randomly assigned to the deferred treatment group in MGT-RPGR-021. A target of 51 to 60 participants will be enrolled in this study, with 10 participants expected to be enrolled in Belgium. AAV5-hRKp.RPGR will be administered to patients via the subretinal space following a standard surgical vitrectomy. The overall objective is to see whether a healthy version of the RPGR gene delivered to the retina by injection during a surgery can correct the defect and improve vision or stop the deterioration of vision.

The assessment of the potential risk for the human health and the environment linked to the deliberate release

Administration of AAV5-hRKp.RPGR will occur only within contained clinical sites by trained medical professionals. The clinical vector AAV5-hRKp.RPGR is replication incompetent by design and will not contain any replication-competent (helper) virus sequences. Viral shedding from patients who receive AAV5-hRKp.RPGR as part of the clinical trial will be closely monitored. Even if release would occur, the GMO will not be able to spread in the environment. In the case of accidental exposure and transfer of vector to an unintended human or non-human recipient, the risks are considered negligible since the

vector is not able to replicate, is not known to be pathogenic, and the amount of particles is unlikely to cause significant infections in the exposed individual. Therefore, environmental impact of AAV5-hRKp.RPGR is considered to be negligible

The proposed measures to limit the potential risk, to control and ensure follow-up of the deliberate release

AAV5-hRKp.RPGR will be administered at clinical trial sites by trained healthcare professionals following local rules for handling and disposal of genetically modified organisms and biological hazards. All patients will be monitored for adverse events as detailed in the clinical trial protocol.

Considering the negligible risk for the environment, no specific plans for protecting the environment are deemed necessary. However, viral shedding from patients who receive AAV5-hRKp.RPGR as part of the clinical trial will be closely monitored.

Date and Location of Release

The proposed treatment and follow up of patients with AAV5-hRKp.RPGR will take place at **UZ Gent, Corneel Heymanslaan 10, 9000 Gent, Belgium** between March 2022 – December 2023 for MGT-RPGR-021 and MGT-RPGR-022.