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

Genetically Modified Organism

Janssen-Cilag International NV 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), AAVCAGsCD59, for the conduct of clinical trial:

- **81201887MDG2001**: A Phase 2b, Randomized, Double-masked, Multicenter, Dose-ranging, Sham-controlled Clinical Trial to Evaluate Intravitreal JNJ-81201887(AAVCAGsCD59) Compared to Sham Procedure for the Treatment of Geographic Atrophy (GA) Secondary to Age-related Macular Degeneration (AMD)

Description of the genetically modified organism

The investigational gene therapy, AAVCAGsCD59, is a recombinant adeno-associated

virus serotype 2 (rAAV2) with a transgene encoding soluble CD59 (sCD59).

AAVCAGsCD59 is currently being developed for participants 60 years of age or older with geographic atrophy (GA) secondary to age-related macular degeneration (AMD).

The Purpose of the proposed Deliberate Release

The purpose of clinical trial 81201887MDG2001 is to study AAVCAGsCD59 for the treatment of geographic atrophy secondary to age-related macular degeneration. A target of 300 participants will be enrolled in this study, with 10 participants expected to be enrolled in Belgium. AAVCAGsCD59 will be administered to patients by intravitreal injection. The overall objective is to see if AAVCAGsCD59 is safe and useful for treating patients with geographic atrophy secondary to age-related macular degeneration.

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

Administration of AAVCAGsCD59 will occur only within contained clinical sites by trained medical professionals. The clinical vector AAVCAGsCD59 is unable to replicate independently even in the presence of a replication-competent (helper) virus. Viral shedding from patients who receive AAVCAGsCD59 as part of the clinical trial will be monitored as outlined in the protocol. 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, recombinant adeno-associated virus (rAAV) vector genomes integrate into host chromosomes at a very low frequency, 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 AAVCAGsCD59 is considered to be negligible

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

AAVCAGsCD59 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 AAVCAGsCD59 as part of the clinical trial will be monitored.

Date and Location of Release

The proposed treatment and follow up of patients with AAVCAGsCD59 will take place at the following sites between August 2023 – February 2025.

- UZ Gent: Corneel Heymanslaan 10, 9000 Gent
- UZ Leuven Gasthuisberg: Herestraat 49, 3000 Leuven
- CHU Liège: Avenue de L'Hòpital 1, 4000 Liège
- ZNA Middelheim: Lindendreef 1, 2020 Antwerpen
- Ziekenhuis Oost-Limburg: Schiepse Bos 6, 3600 Genk