PART 1 (COUNCIL DECISION 2002/813/EC)

SUMMARY NOTIFICATION INFORMATION FORMAT FOR THE RELEASE OF GENETICALLY MODIFIED ORGANISMS OTHER THAN HIGHER PLANTS IN ACCORDANCE WITH ARTICLE 11 OF DIRECTIVE 2001/18/EC

A. GENERAL INFORMATION

1. Details of notification

a) Member State of notification: Belgium

b) Notification number: B/BE/25/BVW8

c) Date of acknowledgement of notification: N/A

d) Title of the project

A Phase 3, Multicenter, Randomized, Double-Blind, Placebo-Controlled Study to Investigate the Efficacy of a Single Intravenous Dose of SGT-003 in Ambulant Males With Duchenne Muscular Dystrophy

e) Proposed period of release: 02Feb 2026 – 31Dec 2033

2. Notifier

Name of institution or company

Solid Biosciences Inc., 500 Rutherford Ave., 3rd Floor, Charlestown, MA, 02129, USA

3. GMO characterization

a) Indicate whether the GMO is a:

Viroid	☐
RNA virus	☐
DNA virus	☒
bacterium	☐
fungus	☐
animal	
- mammals	☐
- insect	☐
- fish	☐
-other animal	☐

other, please specify phylum, class

b) Identity of the GMO (genus and species)

Family:	Parvoviridae
Genus:	Dependoparvovirus
Species:	Recombinant adeno-associated viral vector (AAV)
Strain:	AAV-SLB101 derived from naturally occurring AAV9 serotype

c) Genetic stability – according to Annex IIIa, II, A(10)

AAV is a single stranded DNA virus that demonstrates a high degree of genetic stability as evidenced by the high degree of sequence conservation of the rep and cap genes from multiple AAV serotypes and genomovars. Sequence homologies often are >90% and >80% for the rep and cap genes, respectively. Furthermore, AAV uses host DNA polymerases for viral replication, which are characterized by high fidelity DNA polymerization and additional proofreading exonuclease activity leading to very low error rate of DNA replication, when compared, for example, to RNA polymerases used by RNA viruses. In support of genetic stability is the observation that AAV proviral DNA episomes, isolated from multiple human tissue samples, consistently have the expected canonical AAV2 rep and cap sequences. It is known that wild type AAV DNA as well as that of AAV-based vectors persists in transduced cells as circular (extrachromosomal) episomal concatemers in human tissues.

The genetic stability of SGT-003 is expected to be equivalent to wild type AAV. Due to the lack of viral rep and cap genes, SGT-003 is replication-incompetent and expected to remain in cells as episomes.

4. Is the same GMO release planned elsewhere in the Community (in conformity with Article 6 (1)), by the same notifier?

Yes ☒ No ☐

If yes, insert the country code(s): DE, ES, FR, IT, NL

5. Has the same GMO been notified for release elsewhere in the Community by the same notifier?

Yes ☒ No ☐

If yes:

– Member State of notification: IT

– Notification number: RM/IC/Op1/25/001

Please use the following country codes:

Austria AT; Belgium BE; Germany DE; Denmark DK; Spain ES; Finland FI; France FR; United Kingdom GB; Greece GR; Ireland IE; Iceland IS; Italy IT; Luxembourg LU; Netherlands NL; Norway NO; Portugal PT; Sweden SE

6. Has the same GMO been notified for release or placing on the market outside the Community by the same or other notifier?

Yes ☒ No ☐

If yes:

– Member State of notification: United States; Canada; United Kingdom

– Notification number: IND 29667; NSN 21837; IRAS ID 1010251

7. Summary of the potential environmental impact of the release of the GMOs

SGT-003 is a replication-incompetent recombinant AAV containing the h-μD5 microdystrophin gene for the treatment of patients with Duchenne muscular dystrophy.

The potential for environmental impact of the release of SGT-003 under the conditions of the clinical protocol is negligible for the following reasons:

1. Lack of pathogenicity of the parental virus and the GMO: Despite an estimated seroprevalence of up to 80% for some common human serotypes, no pathogenic effects of wild-type AAV have been identified. The modifications which have led to the generation of the SGT-003 have not raised the pathogenicity.
2. Replication-incompetent GMO: SGT-003 is a non-pathogenic, recombinant AAV vector that lacks all AAV viral genes and cannot replicate even in the presence of a helper virus. SGT-003 replication could only occur in the extremely unlikely event of a transduced host cell being co-infected by wild-type AAV and a helper virus such as human adenovirus or herpes simplex virus (triple infection). In addition, the IMP is confirmed negative for the presence of replication-competent AAVs before being released for use. The GMO is therefore biologically contained and not able to proliferate and spread in the environment.
3. Minimal risk of transmission by virus shedding: SGT-003 is replication incompetent and is not expected to survive, multiply or disperse if it were eliminated intact from the treated patient. AAV-based gene therapies are known to shed via bodily fluids. It has been shown consistently that vectors are shed for a short period of time, but then become undetectable in bodily fluids. The viral load shed in bodily fluid is expected to be low, compared to the necessary dose required to achieve an efficient transduction and detectable gene expression.

   Similar to other AAV-based products, SGT-003 is shed at low levels through bodily fluids and feces after administration. Viral vector shedding matrices will be collected and may be assessed as part of the Phase 3 clinical study.
4. Minimal risk associated with the transgene: SGT-003 is a non-pathogenic recombinant AAV that does not contain any viral genomic sequences, except ITRs (inverted terminal repeats), which facilitate transgene expression and do not lead to production of viral proteins, particles, or DNA replication. Comprehensive toxicity studies failed to demonstrate any toxic effect of SGT-003 at the intended dose. The protein encoded by the transgene is derived from a naturally occurring protein and is therefore unlikely to be toxic to humans or other organisms. No genes for toxins, potential oncogenes, antibiotic resistance, growth factors or other genes that could be potentially harmful have been inserted into SGT-003.

B. INFORMATION RELATING TO THE RECIPIENT OR PARENTAL ORGANISMS FROM WHICH THE GMO IS DERIVED

1. Recipient or parental organism characterization:

a) Indicate whether the recipient or parental organism is a:

Viroid	☐
RNA virus	☐
DNA virus	☒
bacterium	☐
fungus	☐
animal	
- mammals	☐
- insect	☐
- fish	☐
-other animal	☐

other, please specify phylum, class

2. Name

(i)	Order and/or higher taxon (for animals)	Parvoviridae Family
(ii)	Genus	Dependoparvovirus
(iii)	Species	Adeno-associated virus
(iv)	Subspecies	N/A
(v)	Strain	Serotype 9
(vi)	pathovar (biotype, ecotype, race, etc.)	N/A
(vii)	common name	AAV9

3. Geographical distribution of the organism

a) Indigenous to, or otherwise established in, the country where the notification is made:

Yes ☒ No ☐ Not known ☐

b) Indigenous to, or otherwise established in, other EC countries:

(i) Yes ☒

If yes, indicate the type of ecosystem in which it is found:

Atlantic	☒
Mediterranean	☒
Arctic	☒
Alpine	☒
Continental	☒

(ii) No ☐

(iii) Not known ☐

c) Is it frequently used in the country where the notification is made?

Yes ☐ No ☒

d) Is it frequently kept in the country where the notification is made?

Yes ☐ No ☒

4. Natural habitat of the organism

(a) If the organism is a microorganism

Water	☐
soil, free-living	☐
soil in association with plant-root systems	☐
in association with plant leaf/stem systems	☐
in association with animals	☐
other (specify)	In association with animals (primate hosts)

(b) If the organism is an animal: natural habitat or usual agroecosystem:

Not applicable

5. a) Detection techniques

AAVs can be detected using both immunological techniques (ELISA) and polymerase chain reaction (PCR) techniques.

b) Identification techniques

AAVs can be identified by PCR, mass spectrometry, and next generation sequence (NGS) techniques.

6. Is the recipient organism classified under existing Community rules relating to the protection of human health and/or the environment?

Yes ☐ No ☒

If yes, specify

Not applicable

7. Is the recipient organism significantly pathogenic or harmful in any other way (including its extracellular products), either living or dead?

Yes ☐ No ☒ Not known ☐

Additional information: Wild-type AAV is non-pathogenic and has not been classified under Directive 2000/54/EC of the European Parliament and of the Council of 18 September 2000 on the protection of workers from risks related to exposure to biological agents at work. AAVs have no known pathogenic effects, even though the estimated seroprevalence of some common human serotypes is up to 80%. Consequently, AAV

fulfils the definition of a Risk Group 1 biological agent according to Directive 2000/54/EC (a biological agent that is unlikely to cause human disease).

If yes:

a) to which of the following organisms: humans ☐
animals ☐
plants ☐
other ☐

Not applicable

b) give the relevant information specified under Annex III A, point II. (A)(11)(d) of Directive 2001/18/EC

Not applicable

8. Information concerning reproduction

a) Generation time in natural ecosystems:

In nature, wild-type AAV requires the presence of a helper virus, such as adenovirus, to allow replication. Therefore, its generation time is variable depending on the presence of the helper virus.

b) Generation time in the ecosystem where the release will take place:

Same as above.

c) Way of reproduction: Sexual ☐ Asexual ☒

d) Factors affecting reproduction:

Wild-type AAVs are replication defective. The presence of a helper virus such as an adenovirus or a herpes simplex virus in the same cell as the AAV is required for AAV gene expression, genome replication and production of virions.

Please note that the GMO, SGT-003, being a recombinant AAV that lacks the viral rep and cap genes, requires the presence of both wild-type AAV and a helper virus for replication. In the absence of either, SGT-003 is replication-incompetent (see section E.1.b).

9. Survivability

a) Ability to form structures enhancing survival or dormancy:
(i) endospores ☐
(ii) cysts ☐
(iii) sclerotia ☐
(iv) asexual spores (fungi) ☐
(v) sexual spores (fungi) ☐
(vi) eggs ☐
(vii) pupae ☐

(viii) larvae ☐
(ix) other, please specify AAV does not form survival structures. In the absence of a helper virus, wild-type AAV establishes a latent infection by persisting in the host cells as episomal concatemer or, on rare occasions, by integrating into the host cell DNA.

b) Relevant factors affecting survivability:

AAV does not form survival structures but can remain infectious for at least a month at room temperature. Parvoviruses such as AAV are stable viruses that can persist in the environment for extended periods of time (thought to be in the order of several weeks). AAV particles are resistant to a wide range of pH (3 – 9) and can resist elevated temperatures (55ºC for 1 hour). However, as with all viruses, replication of AAV cannot occur outside of a host cell. Additionally, AAV are susceptible to commonly available chemical disinfectants (e.g., sodium hypochlorite) and heat inactivation (e.g,, autoclaving).

10. a) Ways of dissemination

AAV may be transmitted through direct or indirect contact. AAV may be transmitted through inhalation, ingestion, and possible sexual transmission.

b) Factors affecting dissemination

Replication of wild-type AAV requires the presence of a helper virus (e.g., adenovirus or herpes simplex virus). The GMO, SGT-003, is replication deficient even in the presence of a helper virus and, as such, is not expected to replicate or spread through the environment.

11. Previous genetic modifications of the recipient or parental organism already notified for release in the country where the notification is made (give notification numbers)

The sponsor has not notified any previous genetic modifications of the parental AAV9 virus for release in Belgium.

C. .INFORMATION RELATING TO THE GENETIC MODIFICATION

1. Type of the genetic modification

(i) Insertion of genetic material ☒
(ii) Deletion of genetic material ☒
(iii) Base substitution ☐
(iv) Cell fusion ☐
(v) Other, please specify

2. Intended outcome of the genetic modification

The vector genome sequence was modified to generate a recombinant AAV vector lacking the wild-type AAV *rep* and *cap* viral genes so that the vector would be

replication incompetent and provide a template within AAV2 ITRs to introduce the expression cassette coding for the transgene which includes a muscle-specific control element and the coding sequence for the 5-repeat human microdystrophin (h-μD5) intended to treat Duchenne muscular dystrophy (DMD).

In addition, the naturally occurring capsid protein sequence of the AAV9 serotype was modified to create AAV-SLB101 to improve muscle tropism, as it is critical that the AAV target muscle tissue for the treatment of DMD.

3. a) Has a vector been used in the process of modification?

Yes ☒ No ☐

If no, go straight to question 5.

b) If yes, is the vector wholly or partially present in the modified organism?

Yes ☒ No ☐

If no, go straight to question 5.

4. If the answer to 3 b) is yes, supply the following information

a) Type of vector

plasmid	☒
bacteriophage	☐
virus	☐
cosmid	☐
transposable element	☐
other, please specify	

b) Identity of the vector

SGT-003 is produced by a process known as ‘triple transfection’, which utilizes three different plasmid vectors:

1. AAV Vector Genome Plasmid
2. AAV RepCap Plasmid
3. Adenovirus Helper Plasmid

c) Host range of the vector

The plasmids are produced in E.coli (bacterial) cells

d) Presence in the vector of sequences giving a selectable or identifiable phenotype

Yes ☒ No ☐

Antibiotic resistance ☒

Other, specify
Indication of which antibiotic resistance gene is inserted

The three plasmids contain an antibiotic resistance gene allowing for selective amplification of the plasmid in E. coli. The resistance gene is only present in the plasmid backbone and is not packaged into the final GMO and is therefore not present in SGT-003 drug product.

e) Constituent fragments of the vector

SGT-003 is constructed on a batch-by-batch basis by transient transfection of a HEK293 cell line with three plasmids containing the sequences for the generation of recombinant AAV, including the recombinant expression plasmid that contains the expression cassette between 2 ITRs (AAV Vector Genome Plasmid), a plasmid containing the viral replicase and capsid genes (AAV RepCap Plasmid) and plasmid containing the adenovirus helper genes. The three plasmids also contain a bacterial origin of replication and the gene for kanamycin resistance to allow for production of the plasmid in *E. coli* bacterial cells. However, only the recombinant expression cassette will be contained in the final GMO as genetic sequence. The viral proteins will constitute the capsid and the helper genes are only utilized in the packaging of the vector.

f) Method for introducing the vector into the recipient organism

(i) transformation ☐
(ii) electroporation ☐
(iii) macroinjection ☐
(iv) microinjection ☐
(v) infection ☐
(vi) other, please specify Transient transfection

The SGT-003 recombinant AAV vector is produced by a process known as ‘triple transfection’, which utilizes the three plasmids presented above.

5. If the answer to question B.3 (a) and (b) is no, what was the method used in the process of modification?

(i) transformation ☐
(ii) microinjection ☐
(iii) microencapsulation ☐
(iv) macroinjection ☐
(v) other, please specify

Not applicable

6. Information on the insert

a) Composition of the insert

The packaged rAAV vector genome comprises of a promoter, a transgene encoding functional domains of the human dystrophin gene and a polyadenylation (PolyA) signal, flanked by modified AAV2 inverted terminal repeats (ITRs).

b) Source of each constituent part of the insert

- ITRs: Wild type AAV serotype 2
- Promoter: Mus musculus
- h-µD5 transgene cDNA: Homo sapiens
- Polyadenylation sequence: Oryctolagus cuniculus

c) Intended function of each constituent part of the insert in the GMO

- ITRs: Required for replication of the rAAV DNA, packaging into virions during the GMO manufacturing process, and second strand DNA synthesis to facilitate gene expression
- promoter: Intended to drive skeletal and cardiac muscle specific gene expression
- h-µD5 transgene cDNA: Contains functional domains of the human dystrophin gene.
- Polyadenylation sequence: Terminates transcription of the SGT-003 microdystrophin gene.

d) Location of the insert in the host organism

- on a free plasmid ☐
- integrated in the chromosome ☐
- other, please specify The insert is in the ssDNA viral genome, between the ITRs.

e) Does the insert contain parts whose product or function are not known?

Yes ☐ No ☒

If yes, please specify

Not applicable

D. INFORMATION ON THE ORGANISM(S) FROM WHICH THE INSERT IS DERIVED (DONOR)

The following information relates to the organism from which the inserted transgene (h-µD5) is derived.

1. Indicate whether it is a:

Viroid ☐
RNA virus ☐
DNA virus ☐
bacterium ☐

fungus	☐
animal	
- mammals	☒
- insect	☐
- fish	☐
-other animal	☐

other, please specify phylum, class

2. Complete name

(i)	order and/or higher taxon (for animals)	Primates
(ii)	family name (for plants)	N/A
(iii)	genus	*Homo*
(iv)	species	*Homo sapiens*
(v)	subspecies	N/A
(vi)	strain	N/A
(vii)	cultivar/breeding line	N/A
(viii)	pathovar	N/A
(ix)	common name	Human

3. Is the organism significantly pathogenic or harmful in any other way (including its extracellular products), either living or dead?

Yes ☐ No ☒ Not known ☐

If yes, please specify the following

a) to which of the following organisms?

Humans	☐
animals	☐
plants	☐
other	☐

Not applicable

b) are the donated sequences involved in any way to the pathogenic or harmful properties of the organism?

Yes ☐ No ☒ Not known ☐

If yes, give the relevant information under Annex III A, point II (A), 11(d):

Not applicable

4. Is the donor organism classified under existing Community rules relating to the protection of human health and the environment, such as Directive 90/679/EEC on the protection of workers from risks related to exposure to biological agents at work?

Yes ☐ No ☒

If yes, please specify

Not applicable

5. Do the donor and recipient organism exchange genetic material naturally?

Yes ☒ No ☐ Not known ☐

After a natural infection with wild-type AAV, viral genomes are mainly present as circular episomes in human cells, but integration into the human genome can also occur with a low frequency.

E. INFORMATION RELATING TO THE GENETICALLY MODIFIED ORGANISM

1. Genetic traits and phenotypic characteristics of the recipient or parental organism which have been changed as a result of the genetic modification

a) Is the GMO different from the recipient as far as survivability is concerned?

Yes ☐ No ☒ Not known ☐

Please specify

The GMO is secreted in bodily fluids and has similar survival and stability to wild-type AAV. The GMO is devoid of any viral genes required for replication, and as such, is unable to replicate in the presence of a helper virus. All AAVs are susceptible to appropriate virucidal disinfectants, such as 1% to 10% sodium hypochlorite (for at least 20 minutes), alkaline solutions at pH >9, 5% phenol, heat (>80ºC for 60 minutes), UV radiation and extreme pH (<2, >12). Effective disinfectants require 20 minutes' contact time.

b) Is the GMO in any way different from the recipient as far as mode and/or rate of reproduction is concerned?

Yes ☒ No ☐ Not known ☐

Please specify

The SGT-003 viral genome has been significantly modified compared to the wild-type virus to render it replication incompetent. The AAV *rep* and *cap* genes have been replaced with a genetically engineered expression cassette, and only the viral ITR sequences, which are non-coding DNA sequences (<300 bp), have been retained.

SGT-003 requires the presence of both a helper virus, such as human adenovirus or herpes simplex virus, and a wild-type AAV in a single cell to replicate (triple infection), which is an extremely rare event.

c) Is the GMO in any way different from the recipient as far as dissemination is concerned?

Yes ☒ No ☐ Not known ☐

Please specify

As SGT-003 replication could only occur in the extremely unlikely event of a host cell being co-infected by both a wild type AAV and a helper virus such as human adenovirus or herpes simplex virus, the likelihood of dissemination of SGT-003 is lower than that of wild type AAV.

d) Is the GMO in any way different from the recipient as far as pathogenicity is concerned?

Yes ☐ No ☒ Not known ☐

Please specify

No pathogenic effects of wild-type AAV in human are known and the removal of the viral *rep* and *cap* genes is expected to further reduce any risk of pathogenicity. The introduction of the

expression cassette encoding the transgene and regulatory sequences is not expected to result in the development of pathogenicity.

2. Genetic stability of the genetically modified organism

AAV is a single-stranded DNA virus that demonstrates a high degree of genetic stability (see Section A.3.c); based on this, SGT-003 is also expected to be genetically stable. The integrity of the vector genome is confirmed at batch release.

3. Is the GMO significantly pathogenic or harmful in any way (including its extracellular products), either living or dead?

Yes ☐ No ☒ Not known ☐

Wild type AAV is non-pathogenic and has not been classified under Directive 2000/54/EC of the European Parliament and of the Council of 18 September 2000 on the protection of workers from risks related to exposure to biological agents at work. AAV has no known pathogenic effects, even though the estimated seroprevalence of some common human serotypes is up to 80%. Consequently, AAV fulfils the definition of a Risk Group 1 biological agent according to Directive 2000/54/EC (a biological agent that is unlikely to cause human disease). The expression cassette does not contain any harmful sequences.

If yes,

a) to which of the following organisms?: humans ☐ animals ☐ plants ☐ other ☐

Not applicable

b) give the relevant information specified under Annex III A, point II (A) (11) (d) and II (C) (2) (i)

Not applicable

4. Description of identification and detection methods

a) Techniques used to detect the GMO in the environment

SGT-003 can be detected using both ELISA and PCR techniques. AAV9 ELISA can be used to detect the viral capsid and ddPCR with primers designed specific to the transgene can be used to detect the genomic DNA.

b) Techniques used to identify the GMO

SGT-003 can be identified by PCR, Mass Spectrometry, and Next Generation Sequencing (NGS) techniques. The transgene can be identified using PCR with primers designed specifically for the genomic DNA. NGS can also be used to identify the transgene by sequencing the entire genomic DNA and aligning that to the expected DNA sequence. The

capsid can be identified using LC-MS to map the peptide sequence of the capsid proteins and aligning to the expected sequence.

F. INFORMATION RELATING TO THE RELEASE

1. Purpose of the release (including any significant potential environmental benefits that may be expected)

Phase 3, pediatric gene therapy study with SGT-003 in subjects with Duchenne muscular dystrophy. No potential environmental benefit is expected.

2. Is the site of the release different from the natural habitat or from the ecosystem in which the recipient or parental organism is regularly used, kept or found?

Yes ☐ No ☒

If yes, please specify

Not applicable

3. Information concerning the release and the surrounding area

a) Geographical location (administrative region and where appropriate grid reference):

The participating sites in this clinical trial are:

- UZ Leuven, 3000 Leuven, Belgium
- University Childrens Hospital Queen Fabiola, 1020 Bruxelles, Belgium

b) Size of the site (m^2):

(i) actual release site (m^2): Not applicable. A specific size for the site of release cannot be defined as SGT-003 will be administered to patients as part of a clinical trial.

(ii) wider release area (m^2): Not applicable.

c) Proximity to internationally recognized biotopes or protected areas (including drinking water reservoirs), which could be affected:

Administration of SGT-003 will only occur in an appropriate and qualified setting and is therefore not expected to come into contact with any recognized biotopes or protected areas.

d) Flora and fauna including crops, livestock and migratory species which may potentially interact with the GMO

Administration of SGT-003 will only occur in an appropriate and qualified setting and is therefore not expected to come into contact with plants or animals.

4. Method and amount of release

a) Quantities of GMOs to be released:

SGT-003 will be administered intravenously in patients with a one-time dose (1.0E14 vg/kg) for the treatment of Duchenne muscular dystrophy (DMD). Approximately 80 patients will be dosed globally with SGT-003 in this study and 6 patients are anticipated to be administered SGT-003 in Belgium

It is expected that the GMO will be released by shedding in bodily fluids in very small quantities during the days and weeks following administration. Clinical shedding results are expected to be negative in most matrices after Day 90.

b) Duration of the operation:

The administration procedure, including preparation of the infusion system, is expected to take approximately 2 hours.

c) Methods and procedures to avoid and/or minimize the spread of the GMOs beyond the site of the release

Preparation and administration of SGT-003 will take place in an appropriate and qualified setting. The sponsor will provide a Pharmacy Manual that gives directions on use, storage and destruction of the IMP.

SGT-003 must be stored in frozen conditions, in a securely locked area, accessible to authorized persons only, until needed for dose preparation. In-house transport of the IMP will take place in a desinfectable, closed, leakproof, and unbreakable container

Healthcare professionals handling SGT-003 will be trained in biosafety practices to use during the preparation of SGT-003 in the pharmacy, transport to the administration room and precautions during administration. Staff will follow the waste and disposal policies as per local site requirement to dispose of consumables used in the preparation and administration of SGT-003.

Healthcare professionals should use appropriate personal protective equipment (to include gloves, safety goggles, laboratory coat and sleeves) when handling or administering the product. As this is a standard infusion procedure, no additional biosafety precautions have been identified.

The administration room will be cleaned according to the local standard institutional procedures after the administration of SGT-003 to the patient. It is not expected that SGT-003 will be deliberately released into the environment outside of the administration site.

Unused SGT-003 drug product will be disposed of on site as biohazardous waste in accordance with the clinical site’s institutional policies. Documentation of traceability and disposal of the product will be generated and filed at the site.

The risks related to the release into the environment of the GMO or risks to personnel in the event there is a breach in container integrity and/or storage or accidental spillage at the site or during shipping/storage, is considered to be negligible. In the event that a spillage did occur, the product is non-pathogenic and non-replicative, limiting spread and risks to the environment or personnel. The spill will be contained, and the area will be decontaminated using a viricidal disinfectant as per local guidelines and institutional procedures.

5. Short description of average environmental conditions (weather, temperature etc.)

Not applicable. Administration of SGT-003 will occur only in an appropriate and qualified setting (e.g., with access to in-patient unit, ICU level of care, and access to recommended rescue medications) with ambient conditions expected.

6. Relevant data regarding previous releases carried out with the same GMO, if any, specially related to the potential environmental and human health impacts from the release

Study SGT-003-301 is a randomized, double-blind, placebo-controlled study evaluating a single intravenous infusion of SGT-003 in pediatric male participants with Duchenne muscular dystrophy (DMD). The potential benefits of SGT-003 treatment are based on the findings from nonclinical studies and initial clinical data from the first-in-human study, SGT-003-101. The nonclinical findings include evidence of microdystrophin expression and membrane localization across skeletal and cardiac muscle tissues, the restoration of dystrophin-associated protein complex members to the muscle membrane, and improved muscle function in a dystrophin negative animal model of DMD treated with SGT-003. As a result, potential benefits following the administration of SGT-003 include slowing the progression of the disease by preserving motor abilities.

Based on clinical experience with SGT-003, and clinical data from known AAV9-based products, the environmental impact is expected to be negligible.

G. INTERACTIONS OF THE GMO WITH THE ENVIRONMENT AND POTENTIAL IMPACT ON THE ENVIRONMENT, IF SIGNIFICANTLY DIFFERENT FROM THE RECIPIENT OR PARENT ORGANISM

1. Name of target organisms (if applicable)

(i)	order and/or higher taxon (for animals)	Primates
(ii)	family name (for plants)	N/A
(iii)	genus	*Homo*
(iv)	species	*Homo sapiens*
(v)	subspecies	N/A
(vi)	strain	N/A
(vii)	cultivar/breeding line	N/A
(viii)	pathovar	N/A
(ix)	common name	Human

2. Anticipated mechanism and result of interaction between the released GMOs and the target organism (if applicable)

The target organism is the human participant enrolled in the clinical trial. Duchenne muscular dystrophy affects all skeletal muscles in the body, in addition to the diaphragm and heart. As such, a systemic approach is necessary in order to provide the best possible prospect of direct

benefit to patients. Utilizing the AAV-SLB101 capsid serotype allows for efficient transduction of cardiac, skeletal and diaphragm muscle.

SGT-003 contains cDNA encoding a five-repeat human microdystrophin (h-μD5). The transgene expression is driven by muscle-specific promoter. It is expected that the administration of SGT-003 will result in expression of the transgene primarily in cardiac and skeletal muscle tissues. Since SGT-003 does not encode proteins that aid integration into the host genome, the rAAV are expected to persists extra chromosomally as episomes in muscle cells.

3. Any other potentially significant interactions with other organisms in the environment

Persons other than the human subjects receiving the medicinal product will not be exposed to significant levels of SGT-003. Exposure, such as environmental exposure, is expected to be minimal (see risk minimization strategy in sections F.4.c, I. and J.). As SGT-003 is replication incompetent, it is expected that any vector would be rapidly cleared from any non-target organisms without causing any harmful effects.

4. Is post-release selection such as increased competitiveness, increased invasiveness for the GMO likely to occur?

Yes ☐ No ☒ Not known ☐

Please give details

As SGT-003 is unable to replicate, post-release selection cannot occur.

5. Types of ecosystems to which the GMO could be disseminated from the site of release and in which it could become established

As SGT-003 is unable to replicate, it is not expected to spread to the environment to a significant degree, and it is not expected to become established in any ecosystems.

6. Complete name of non-target organisms which (taking into account the nature of the receiving environment) may be unintentionally significantly harmed by the release of the GMO

(i)	order and/or higher taxon (for animals)	N/A
(ii)	family name (for plants)	N/A
(iii)	genus	N/A
iv)	species	N/A
(v)	subspecies	N/A
(vi)	strain	N/A
(vii)	cultivar/breeding line	N/A
(viii)	pathovar	N/A
(ix)	common name	N/A

7. Likelihood of genetic exchange in vivo

a) from the GMO to other organisms in the release ecosystem:

It is expected that SGT-003 vector genome will be transferred into tissues within the body of patients. As SGT-003 is replication-incompetent and is only expected to be shed in trial subjects' bodily fluids to a limited extent, transmission and gene transfer to organisms other than the study subjects is considered unlikely.

b) from other organisms to the GMO:

Not expected. The probability of homologous recombination with related viruses that could lead to variants of the GMO is strongly reduced with the ITRs being the only viral sequences remaining in the vector. It is not expected that any organism's DNA could be transferred to the viral episomes and be incorporated into the SGT-003 DNA genome.

c) likely consequences of gene transfer:

Negligible. Recombination between SGT-003 and a wild-type AAV would lead to the formation of viruses that are, similarly to the recombinant AVV, replication incompetent. Gene transfer from the GMO to another organism could lead to the expression of the human microdystrophin transgene.

8. Give references to relevant results (if available) from studies of the behaviour and characteristics of the GMO and its ecological impact carried out in simulated natural environments (e.g. microcosms, etc.):

No such studies have been conducted with SGT-003.

9. Possible environmentally significant interactions with biogeochemical processes (if different from the recipient or parental organism)

SGT-003 is not known or predicted to have an impact on biogeochemical processes.

H. INFORMATION RELATING TO MONITORING

1. Methods for monitoring the GMOs

Biodistribution and viral shedding samples (muscle, blood, urine, saliva, and feces) will be collected from participants at post-dosing timepoints and may be assessed by a PCR assay that detects the genomic sequence of the microdystrophin transgene in SGT-003.

2. Methods for monitoring ecosystem effects

None. No monitoring of the environment is planned since the risk to the environment is considered negligible.

3. Methods for detecting transfer of the donated genetic material from the GMO to other organisms

Transfer of genetic material from SGT-003 to other organisms is negligible.

qPCR/ddPCR can be used for detecting transfer of the donated genetic material from the GMO to other organisms, if needed.

4. Size of the monitoring area (m^2)

Not applicable; monitoring techniques will only be used with regards to the trial patients.

5. Duration of the monitoring

Biodistribution and viral shedding will be collected from participants up to the 1-year post-treatment timepoint.

6. Frequency of the monitoring

Biodistribution and viral shedding will be collected frequently in the first month following SGT-003 administration and will continue on a less frequent basis up to the 1-year post-treatment timepoint.

I. INFORMATION ON POST-RELEASE AND WASTE TREATMENT

1. Post-release treatment of the site

After administration of the SGT-003 to the patients, the procedure room will be disinfected using an appropriate disinfectant as per the pharmacy and dose administration manuals and local guidelines for handling of biological waste.

2. Post-release treatment of the GMOs

Any opened and/or unopened SGT-003 will be destroyed on site according to local procedures in a manner consistent with the standard practice of the institution for BSL-1 GMOs. In the medical facility, this will involve temporary containment in sharps bins or clearly marked bags (e.g. biohazard, medical waste) prior to autoclaving and/or incineration either on or off site.

3. a) Type and amount of waste generated

After administration of SGT-003, the following waste is generated; empty vials, used vials, guide tube, cannula, injection needles and syringes, gauzes, gloves, and components used for collecting body fluids samples.

3. b) Treatment of waste

All materials that may have come in contact with SGT-003 must be disposed of in accordance with local guidelines on handling of biological waste. In the medical facility, this will involve temporary containment in sharps bins or clearly marked bags (e.g. biohazard, medical waste) prior to autoclaving and/or incineration either on or off site. The waste is removed from site by a third party vendor approved by the clinical facility.

J. INFORMATION ON EMERGENCY RESPONSE PLANS

1. Methods and procedures for controlling the dissemination of the GMO(s) in case of unexpected spread

In case of accidental spillage of SGT-003, the spill will be contained, and the area will be decontaminated using a viricidal disinfectant as per local guidelines and institutional procedures. A spill kit will be available at all times during all the steps, but at a minimum during the dose preparation and administration procedure. Healthcare professionals should ensure suitable personal protection during removal of spillages.

Contaminated liquids will be disposed of as biohazardous waste as per local guidelines and institutional procedures. These procedures may include:

- Evacuate area, remove contaminated personal protective equipment (PPE) and allow agents to settle for a minimum of 30 minutes. Initiate spill response procedure.
- Cover the spill with absorbent material. Starting at the edges and work towards the center.
- Carefully pour disinfectant (fresh 10% bleach solution followed by alcohol wipes) over the absorbed spill, again starting at the edges. Saturate the area with disinfectant.

- Allow sufficient contact period to inactivate the material in the spill. Non-viscous spills require 15-20 minutes: viscous spills require 30 minutes.
- Use paper towels to wipe up the spill, working from the edge to center. Use tongs or forceps to pick up broken plastics, glass or other sharps that could puncture gloves.
- Discard absorbent material in biological waste bags.
- Clean the spill area with fresh paper towels soaked in disinfectant. Thoroughly wet the spill area, allow to disinfect for 15-20 minutes longer, and wipe with towels. Discard all cleanup materials (soaked with disinfectant) in a Chemical bag/container, and any contaminated PPE in a biohazard bag. Close and secure the bags.
- Place bag in a second biohazard bag, secure and dispose as per institutional guidelines for biohazardous waste.

2. Methods for removal of the GMO(s) of the areas potentially affected

Any surface area exposed to SGT-003 will be disinfected using appropriate disinfectant as per local guidelines and institutional policies and procedures. All materials used in the clean-up will be discarded as biohazardous waste and will be incinerated.

3. Methods for disposal or sanitation of plants, animals, soils etc. that could be exposed during or after the spread

Administration of SGT-003 will only occur in an appropriate and qualified clinical setting. Therefore, it is not expected that it will come into contact with plants, animals or soil. Furthermore, SGT-003 is not capable of infecting plants or microbes.

4. Plans for protecting human health and the environment in the event of an undesirable effect

Healthcare professionals will follow local laws and institutional procedures for the handling and disposal of genetically modified organisms. Considering the negligible environmental risk of SGT-003, no specific plans for protecting human health and the environment are deemed necessary.

All patients will be carefully monitored for any adverse reactions during this study. An external data and safety monitoring board (DSMB) will be responsible for monitoring safety data from the study.