M.A.G.I.C. Clinic LTD

Meeting Date:	April 10, 2025, 10:00 AM Mountain Time
Institution:	M.A.G.I.C. Clinic LTD, Calgary, AB, Canada
PI:	Aneal Khan, MD
Sponsor:	Spur Therapeutics Limited
Protocol:	FLT201-03: A Phase 3 Safety and Efficacy Trial of FLT201 Gene Therapy in Patients with Gaucher Disease Type 1
Meeting Type:	Initial Review (Protocol and Site)

Present:	Nicholas Noriea (Chair), Joanna Spinato, Daniel Rastein, Deanna Renyk, Elizabeth Kornaga, Deanna Maynard (Site Contact, non-voting)
Guests:	Ahmad Shaheen, Aneal Khan (joined at 10:19 AM MT)
Staff:	Jennifer Smith
Absent:	All other Rostered members not listed as present were absent from the meeting.

1) **Call to Order:** 10:01 AM Mountain Time
   a) Introductions: The roll of attendees was read, and the Chair provided an overview of the review process.
   b) Public Posting: The Site confirmed that a public meeting notice was posted. No comments or questions were received by the Site.
   c) Conflict of Interest: None reported by voting members of the IBC.

2) **Review of Prior Business**: Approval of meeting minutes

   Khan, ST-920-201, AN.CIR, 12-14-23
   Discussion of the minutes: None
   Motion: To approve the minutes as written
   For: 5
   Against: 0
   Abstain: 0

3) **Protocol Overview:**
   a) Primary Reviewer: Nicholas Noriea
   b) Applicable NIH Guidelines: Section III-C
   c) Trial Overview: FLT201-03 (GALILEO-3) is a non-randomized Phase III study sponsored by Spur Therapeutics Limited and designed to assess the efficacy and safety of FLT201 in adult participants with Gaucher disease Type 1 on stable treatment with enzyme replacement therapy (ERT) or substrate reduction therapy (SRT) for at least 2 years. The study agent FLT201 is a recombinant, replication-defective adeno-associated viral (AAV) vector expressing the human lysosomal enzyme β-glucocerebrosidase (GCase). This trial has a target enrollment of 45 participants who will receive a single intravenous infusion of FLT201 at a dose of 4.5E11 vector genome per kilogram bodyweight (vg/kg). Following dosing, participants will receive prophylactic immunosuppressants to mitigate risks of vector-associated transaminitis. Clinical samples including blood, urine, and semen may be collected throughout the study for medical and study-related assessments including viral shedding and immune response to the AAV capsid. Participants will be followed for 5 years after agent administration.
   d) Investigational Study Agent: The study agent FLT201 is a recombinant, replication-incompetent single-stranded AAV vector with a novel engineered synthetic viral capsid, AAVS3, derived from wild-type AAV3B and AAV8 and selected based on its ability to

preferentially transduce human hepatocytes with high efficiency and specificity. The FLT201 genome consists of inverted terminal repeats (ITRs) from AAV2 flanking an expression cassette consisting of liver-specific promoter FRE76, SV40 intron, GCase transgene, and bovine growth hormone polyadenylation sequence. The transgene consists of a codon-optimized human β-glucocerebrosidase variant 85 incorporating two amino acid substitutions to increase enzymatic stability in various physiological conditions. The FLT201 AAV vector is produced in the absence of a helper virus by transient transfection of 293T human embryonic kidney cells with plasmids carrying vector genome, adenoviral helper genes, and AAV rep and cap genes.

e) HGT Medical Consultant review: The Consultant confirmed the clinical safety profile presented in the Risk Assessment.

Discussion of the Protocol:

(1) In response to a question from the Site, the Chair clarified the enrollment was described in the protocol as planned number of participants. The Chair further clarified that the Protocol was not designated as country-specific and so the planned enrollment was understood to be global. The Chair further noted that clarification to this regard in the Protocol would need to be submitted by the Institution to the Sponsor.

(2) In response to a question from the Site, the Chair noted that to their knowledge there were no descriptions of adverse physical stress events described in the Investigator's Brochure, but there were several AESIs related to cardiac events. The Site had no additional questions.

Motion: Approval at CL-1 plus Routine Practices

For:	5
Against:	0
Abstain:	0

4) **Site Overview:**

a) The Chair introduced an overview of the facility to the IBC by discussing Site documents provided for Committee review, including areas where study agent will be stored, prepared, administered, and disposed.

b) The Committee discussed the reviewed documents that include but are not limited to: Training Records (IATA and BBP), Emergency Response Plan, Biosafety Manual/ECP, the PI's Credentials.

c) Location: All activities with study agent will be at 215-971 64 Ave NE, Calgary, AB, Canada.

Discussion of the Site:

(1) The Site confirmed the arrangements as described by the Chair are accurate.

(2) After deliberation, while noting that the study could be approved at CL-1 plus routine practices, the Committee approved the Site for this study at CL-2 to allow for consistency in the procedures at the Site with other trials approved at CL-2. The Committee reminded the Site that approval at CL-2 requires they meet CL-2 standards.

(3) In response to a question from the Committee, the Site confirmed that the eyewash stations are all disposable bottles, with wall mounted bottles in the Lab and Pharmacy and portable bottles in the clinic rooms. The Site also confirmed that a procedure is in place to check the expiration dates regularly and replace bottles when used.

(4) In response to a question from the Committee, the Site confirmed that the -80°C freezer is lockable with controlled access to the key.

(5) The Committee noted the spill kit is for chemical spills. The Site confirmed that appropriate PPE and disinfectant are nearby if needed. In response to a question from the Committee, the Site confirmed that they have N95 masks on site and will add them to

the spill kit, so staff can wear them in case of a spill. The Site confirmed that the staff potentially wearing the N95 masks have been fit tested and would have a valid fit test on record. The Committee noted that an SOP is available in the Pharmacy Manual for spills and the Site confirmed that they also have a spill procedure in place.

(6) The Committee noted that the shipping training certificate does not meet the Transport Canada requirements under TDGR Section 6.3 and only includes shipping by air. The Site confirmed the completion date is November 1, 2023, and confirmed that they have both air and ground transportation training. The Committee recommended the Site ensure appropriate shipping training is in place.

(7) In response to a question from the Committee, the Site confirmed that the applicable staff are given site-specific training and the general biosafety training has been refreshed recently. The Committee noted that federal training standards are in the Canadian Biosafety Standard 4.2.2.

(8) In response to a question from the Committee, the Site confirmed that the training certificates are representative certificates for their staff.

(9) In response to a question from the Committee, the Site confirmed that bleach is diluted on-demand and not stored as a diluted solution.

Contingencies as stated by the Chair: None

Recommendations by the IBC:

(1) The Committee recommended the Site ensure appropriate shipping training is in place.

Motion: Approval at CL-2

For:	5
Against:	0
Abstain:	0

5) **Reminder of IBC Approval Requirements:** The Site was reminded of the requirements for IBC approval going forward for the next year.

Please immediately inform CBS if any of the following should occur:

1. Change in the Principal Investigator (PI).
2. Change in the location where the study agent will be stored, prepared, and/or administered to study participants. This will include additional trial sites and onsite/offsite facilities.
3. Changes in the study required personal protective equipment (PPE).
4. New or updated Sponsor Documents must be provided to CBS as soon as they are received. Changes in the study agent formulation (e.g., dosage, carrier liquid, or solvent, method of preparation, or route of administration) must be reviewed by your IBC.
5. Any observed violations of the *NIH Guidelines*, significant research related exposures or incidents (i.e., accidents, spills), or staff illness that could be related to study agent exposure.

Additionally, all study staff must be informed of the potential hazards and risks of working with the study agent and trained to work with the study agent safely. The Principal Investigator should consider encouraging staff to enroll in an occupational health and medical surveillance program, based on the nature of the study agent and its associated risk.

6) **Post Meeting Note:** None

7) **Adjournment:** 11:05 AM Mountain Time