Date: August 1st, 2017

Professor Ibrahim Al Janahi - Executive Director of Research, Medical Research Center
Dr. Mohammed Hammoudeh - Chair of Hamad Medical Corporation IRB
Dr. Mohamed Abdel Daem Yassin - Principal Investigator

This letter is in reference to the clinical trial titled "**A phase 3, Double-blind, Randomized, Placebo-controlled, Multicenter Study of GBT440 Administered Orally to Patients with Sickle Cell Disease**",

The below protocols, submitted on April 25th, 2017 by Hamad Medical Corporation and sponsored by Global Blood Therapeutics, Inc., have been reviewed.

Research proposal	Reviewed Document
17028/17	1) 17028_Assent_Ara_V2_8Feb17_6Pages 2) 17028_Assent_Eng_V2_8Feb17_6Pages 3) 17028_CaregiverTraining_Ara_V2_21Nov16_04Pages 4) 17028_CaregiverTrainingQuiz_Eng-Ara_V1_05Dec16_21Pages 5) 17028_CaregiverTrainingScript_Eng_V2_21Nov16_05Pages 6) 17028_CaseReportForm_V2.0_01Dec16_68Pages 7) 17028_DrugReminders_Ara_V1_18Oct16_01Page 8) 17028_ DrugReminders_Eng_V1_18Oct16_01Page 9) 17028_EveningDiary_Eng-Ara_V1_05Dec16_14Pages 10) 17028_InformedConsentAdultParent_Ara_V2_8Feb17_19Pages 11) 17028_InformedConsentAdultParent_Eng_V2_8Feb17_21Pages 12) 17028_InformedConsentPregnantPartner_Ara_V2_8Feb17_6Pages 13) 17028_InformedConsentPregnantPartner_Eng_V2_8Feb17_6Pages 14) 17028_InitialApplication_15Jan17_07Pages 15) 17028_LabManual_Eng_V2.0_15Dec16_163Pages 16) 17028_MedicationDiary_Eng-Ara_V1_05Dec16_10Pages 17) 17028_ParticipantQuiz_Eng-Ara_V1_05Dec16_30Pages 18) 17028_PatientCard_Ara_V1_18Oct16_01Page 19) 17028_PatientCard_Eng_V1_18Oct16_01Page 20) 17028_PracticeDiary_Eng-Ara_V1_05Dec16_07Pages 21) 17028_Protocol_ V2_19Jan17_87Pages 22) 17028_ProtocolAmendment02_Summary of Changes_19Jan17_02Pages 23) 17028_SCDSeverityMeasure_Eng-Ara_V1_05Dec16_13Pages 24) 17028_SchemeOfDelegation_03Pages 25) 17028_SignedProtocolPage_Amendment02_09Mar17_01Page 26) 17028_SubjectTraining_Ara_V2_21Nov16_05Pages 27) 17028_SubjectTrainingScript_Eng_V2_21Nov16_06Pages

Following the review of the submitted documents, the MOPH supports the conduct of this clinical trial. This support is governed by the compliance of the institution, the DSMB, and the Principal Investigator (PI)) with the below responsibilities. This is to ensure the study is conducted in compliance with MoPH regulations and the principles of International Conference of Harmonization (ICH) - Good Clinical Practice (GCP

Dr. Mohamed Abdel Daem Yassin's responsibility

1. The safety and wellbeing of participants are protected
2. Research involving human subjects begins only after IRB review and approval
3. The research is conducted in accordance with the local IRB-approved protocol, including the approved recruitment number of participants, 8 participants in this study, and consent procedures.
4. Informed consent is obtained and documented before research participation begins
5. All unanticipated problems, including adverse event(s) are reported in accordance with the IRB's policy and MOPH regulations on reporting unanticipated problems including adverse events.
6. All drug logistic is maintained and recorded
7. The protocol's amendments (e.g., protocol, recruitment materials, consent form, status of the study, etc.) is submitted to the IRB for review and approval prior to initiation of the change(s), except where necessary to eliminate hazards to the subject(s). Changes made to eliminate apparent immediate hazards to subjects must be reported to the IRB as unanticipated problem
8. All investigators and study staff listed on the project are informed of changes and unanticipated problems, including adverse events, involving risks to subjects or others
9. The continuing review submission to the IRB should be submitted with sufficient time to allow for IRB review and approval and provide an opportunity for response by the Principal Investigator to any stipulations of the local registered IRB.
10. When the research protocol ends, a final report is submitted to the IRB
11. Adequate and accurate research records are kept and retained
12. The confidentiality of data is maintained at all times
13. Upon request for monitoring and oversight of the research, research records are made available to MoPH, the DSMB, the Global Blood Therapeutics

14. Ensure the study personnel are:

- Qualified by training and experience, and credentialed if necessary, to perform study-related tasks that have been assigned to them.
- Aware of regulatory and policy requirements and standards for the conduct of human subjects research.
- Understanding the details of the protocol relevant to the tasks they will be performing.
- Following the IRB-approved protocol.
- Informed of any pertinent changes to the protocol during the conduct of the study and are educated or given additional training, as appropriate

It is the HMC-IRB's responsibility to:

1. Monitor the safety and wellbeing of research participants
2. Ensure that informed consents are in place
3. Provide enough support to the PI to fulfill his above mentioned responsibilities
4. Protect the privacy and confidentiality of participants.
5. Provide one to one training to involved research staff.
6. Conduct periodic reviews throughout the trial's duration.
7. Conduct continuous monitoring during the conduct of the trials.
8. Report all unanticipated problems including adverse events to the MoPH.
9. Keep IRB meeting minutes, trial recordkeeping, etc. for inspection purposes.

It is the Independent Data and Safety Monitoring Board's responsibility to:

1. Periodically review and evaluate the accumulated study data for participant safety, study conduct and progress, and, when appropriate, efficacy.
2. Make recommendations concerning the continuation, modification, or termination of the trial.
3. Ensure that the timeliness, completeness, and accuracy of the data submitted to them for review are sufficient for evaluation of the safety and welfare of study participants.
4. Report adverse events to the IRB, MOPH, and the sponsor.

For any enquiries, please contact the Research Division at MoPH via: irb@moph.gov.qa

Sincerely yours,

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